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VULNERABLE PLAQUES

SOHAIB AHMAD;NADIA SHIRAZI; M.U. RABBANI

HOW TO DEFINE A VULNERABLE PLAQUE?

The term, *vulnerable plaque*, has been used synonymously with the terms high-risk plaque, thrombosis-prone plaque, thin-cap fibroatheromas (TCFAs), unstable plaque and disrupted plaque and refers to a plaque at increased risk of causing thrombosis and lesion progression[1].

Plaque rupture was first recognized as the initiating event of most cardiovascular diseases in 1966 and has been under extensive study ever since [2].

Prospectively, a vulnerable plaque can be defined as a plaque identified by the technology tested and documented to have a high likelihood of forming a thrombogenic focus. The thrombus could thus produce immediate disease onset, or rapid, asymptomatic, angiographic progression. On the other hand, a plaque with a low likelihood of causing such an outcome would be termed *non-vulnerable*[1].

The American Heart Association (AHA) classifies plaques into six types based on histologic features – Type I (initial changes); type II (fatty streak); type III (pre-atheroma); type IV (atheroma); type V (fibroatheroma); and type VI (complicated plaque) – all thrombosed lesions are included in type VI as complicated lesions[3,4].

CHARACTERISTICS OF A VULNERABLE PLAQUE

Although evidence suggests that certain features can identify vulnerable plaques but no conclusive data exists. The following features in a plaque have been implicated as being predictive of an adverse outcome:[3,4]

A] Large lipid core (40% of the entire plaque)
B] Thin cap
C] Increased macrophage content
D] Increased proteoglycan content
E] Presence of a calcified nodule

There are no prospective studies clearly establishing any particular histologic type as being vulnerable plaque; also it is not possible to identify the frequency of vulnerable plaque due to unavailability of a simple method of identifying such plaques. Autopsy based studies have a certain selection bias, but the best evidence about the frequency of various histologic types of plaques comes from postmortem studies[1].

Three major factors determine the vulnerability of the fibrous cap:[5]

A] Circumferential wall stress or *cap fatigue*
B] Lesion characteristics- location, size and consistency
C] Blood flow characteristics

Platelet disruption involves inflammation as an important adjunct to mechanical factors[8] and activated inflammatory cells have been detected in the disrupted areas of atherectomy specimens from patients with acute coronary syndromes. These inflammatory cells secrete proteolytic enzymes such as matrix metalloproteinases and are capable of degrading the extracellular matrix, affect vascular remodeling and migration of smooth muscle cells across the basement membrane[9].

Lesion thrombogenicity has also been linked with tissue factor content and local tissue factor inhibition reduces lesion thrombogenicity [10]. Evidence also suggests that increased tissue factor expression is associated with cell apoptosis[10].

LESIONS THAT LEAD TO ACUTE CORONARY SYNDROMES

Atleast 65-70% of the atherothrombi are caused by plaque rupture, 25-30% of thrombi occur from plaque erosion and 2-5% of atherothrombi occur as a result of calcified nodules that protrude into the lumen.

I] Plaque Rupture

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Plaque rupture is defined as a necrotic core with a thin fibrous cap that is disrupted or ruptured, allowing the flowing blood to come in contact with the necrotic core. Rupture of the fibrous cap usually occurs in the shoulder regions, the weakest portion where the stress is highest and matrix metalloproteinase production is increased[112].

The frequency of plaque rupture reported in various series of sudden coronary deaths varies from 30% [113] to over 85% [14, 15]. Calcification is present in 80% of plaques that rupture but is usually either speckled or fragmented and infrequently diffuse. The coronary plaques in plaque rupture are equally concentric or eccentric and are more frequent in men and postmenopausal women[116].

2] Plaque Erosion

It is defined as a lesion with luminal thrombus with a base rich in smooth muscle cells and proteoglycan matrix [117] At the site of thrombosis, there is absence of an endothelial layer. These lesions are usually not calcified, or have speckled calcification if calcified [118]. Majority of plaque erosions are eccentric and occur most frequently in young men and women less than 50 years of age and are associated with smoking especially in premenopausal women [19].

3] Calcified Nodule

An infrequent cause of thrombosis in patients dying a sudden cardiac death, it refers to a lesion with a fibrous cap disruption, absence of endothelium and thrombus associated, dense calcified nodule with bone formation. The origin of calcified nodule is thought to be associated with healed plaque ruptures. Mid-right coronary artery accounts for over 50% of the cases because of maximum torsion stress and is the lesion is usually seen in elderly males with heavily calcified and tortuous arteries [120].

4] Thin-cap Fibroatheroma

The thin-cap fibroatheroma (TCFA) has been defined as a lesion with a fibrous cap < 65μm thick and infiltrated by macrophages (>25 cells per 0.3 mm diameter field) [121]. The cap may or may not be eccentric and the necrotic core is well developed. Over 50% of the plaque ruptures, healed plaque ruptures and TCFAs occur in the proximal portions of the major coronary arteries with < 50% diameter stenosis and another third in the mid-portion of these arteries while the rest are distributed in the distal segments [122]. Fifty percent of TCFAs have absent or speckled calcification, and the remainder has a diffuse or a fragmented calcification pattern [118].

DIAGNOSIS OF THE VULNERABLE PLAQUE

Since the consequences of rupture of vulnerable plaque may be catastrophic, their identification is of paramount significance to enable the development of treatment modalities to stabilize such plaques.

a) Coronary Angiography: It is the gold standard for assessment of obstructive lesions but it fails to assess the plaque burden. Also, since 70% of acute coronary occlusions are in areas that were angiographically normal previously, the technique is severely limited in identifying vulnerable plaque.[123]

b) Angioscopy: More sensitive than angiography, it offers direct visualization of the plaque surface and intraluminal structures like tears and color of the thrombi. . However, angioscopy is difficult to perform, is invasive, is associated with a risk of peri-procedural ischaemia and only a limited part of the vessel tree can be investigated.[124]

c) Intravascular Ultrasound (IVUS): Provides real time high-resolution images of the vessel wall and lumen. Only structures over 160 μm can be visualized accurately. Calcification is characterized by a bright echo signal with distal shadows that hide plaque components and deeper vessel structures. The sensitivity of detection of micro-calcification is around 60%[125]. Lipid deposition is described as echoluscent zones and can be detected on IVUS with a sensitivity of between 78 and 95% and specificity of 30% [126]. The sensitivity to differentiate between fatty and fibrous tissue is between 39 and 52% [127]. IVUS assessment of vascular remodeling may help to classify plaques with the highest probability of spontaneous rupture[128].

d) Intravascular Elastography: Based on the concept that upon uniform loading, the local relative amount of deformation of a tissue is related to the local mechanical properties of that tissue, this technique differentiates between hard and soft tissue that may be important for detection of a deformable plaque prone to rupture.

e) Other Techniques:

- Optical Coherence Tomography
- Thermography
- Raman Spectroscopy
- Near-Infrared Spectroscopy
- Magnetic Resonance Imaging
- Shear Stress Imaging

All the techniques are still under development and at present none of them can identify a vulnerable plaque alone or predict its further development. Thus a combination of various modalities will be important in the future to ensure high sensitivity and specificity in detecting vulnerable plaque.

CAN PERIPHERAL BLOOD BE USED TO IDENTIFY VULNERABLE PLAQUES?

Several candidate markers in peripheral blood either singly, or in combination identify patients at high cardiovascular risk – LDL and oxidized LDL, C-reactive proteins and other acute phase reactants, p-selectins, monocyte chemoattractant protein-1 and macrophage colony

stimulating factor, CD-40 ligand, interleukins (1b and 6), matrix metalloproteinases- to name a few. Pregnancy-associated plasma protein is a new marker for vulnerable plaque and is currently under extensive study[129].

THERAPY FOR VULNERABLE PLAQUE

Drugs (Plaque Stabilizers)

- HMG CoA reductase inhibitors (Statins)
- Angiotensin converting enzyme inhibitors (ACEI)
- Antihypertensive agents
- b-blockers
- w-3 fatty acids
- Antiplatelet agents (Aspirin/ Clopidogrel)
- Others

- Peroxisome proliferator activated receptor agonists
- Anti-inflammatory agents
  - Antibiotics
  - Antioxidants

Therapies that may possess plaque-stabilizing effects

Gene therapy

- Metalloproteinase inhibitors
- CD-40 pathway inhibitors

Photodynamic therapy

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Infective endocarditis in the East coast of peninsular Malaysia: a two year retrospective survey from Kuantan.

Rathor Mohammad Yousuf, MD, S H How, M. Med., A R M Fauzi, MRCP, A Shah, Msc

Abstract

Infective endocarditis (IE) remains a life threatening infection that is virtually always fatal if untreated. Despite advances in early diagnosis and treatment, several studies have reported an increase in the incidence of IE with notable changes in the nature of underlying cardiac disease. Degenerative, prosthetic, iatrogenic valvular disease and IE among intravenous drug users (IVDU) are now reported more frequently than rheumatic heart disease. The objective of this study was to determine the frequency of IE, its predisposing factors, microbiological status, and outcome at a state hospital in eastern Malaysia. Sixty seven inpatients diagnosed as IE or suspected IE from June 2000 till July 2002 were identified from hospital records out of which 45 cases that fulfilled the Duke criteria for diagnosis were included in the present study. The patients' predisposing factors, clinical findings, complications, results of investigations and data on clinical outcome were extracted. There were 44 male and 1 female cases with a mean age of 31.9 years, of which 86.7% were IVDUs. Fifteen of our patients were HIV positive, all of whom were IVDU. There was no statistically .significant difference in bacteriology and echocardiography findings among HIV-positive and HIV-negative patients. Among IVDU. *Staphylococcus aureus* was the most common organism (61.5%) followed by streptococci (17.9%). Among non-IVDU, streptococci were isolated in 66.6 % cases, and *Staphylococcus aureus* in 1 case (16.6%). All cases were treated medically and median follow up was 6 months. A successful outcome was seen in 91% of patients.

Conclusion: Intravenous drug use is the commonest predisposing factor for IE among our patients.

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INTRODUCTION:

Infective endocarditis (IE) is an infection of the endocardial surface of the heart and it implies presence of micro-organisms in the lesion[1]. Formerly rheumatic heart disease was the commonest predisposing cause, but mitral valve prolapse, aortic sclerosis, bicuspid aortic valvular heart disease, prosthetic valvular heart disease and intravenous drug use (IVDU) are now more frequently encountered.[2]. In the United States and Western Europe, the incidence of community acquired native-valve endocarditis in most recent studies is 1.7 to 6.2 cases per 100,000 person-years.[3,4] The incidence among IVDU is estimated at 150 to 2000 per 100,000 person-years and can be higher among patients with known valvular heart disease[5]. IE in IVDU has special etiological, epidemiological and clinical characteristics compared to IE in non–IVDU in most studies.[6] The patients tend to be younger, and may be co-infected with human immuno-deficiency virus (HIV). In recent years, Malaysia, like many other countries, has witnessed a considerable increase in drug abuse among young persons. The proximity of Malaysia to the Golden Triangle has greatly contributed to an increased availability of illicit drugs.[7] In 2002, there were 22,008 addicts in the whole country consisting of 11,477 (52.15%) new addicts and 10,531 (47.85%) repeat addicts. The drug addicts are male (almost 99%), in the age group 20-24 years and mostly Ethnic Malays, followed by Chinese and Indians, as well as foreigners.[8]

The aim of this study was to determine the incidence of infective endocarditis, its predisposing factors, microbiological status, and outcome among the local population in a state hospital at Kuantan in the east coast of Malaysia.

Material and methods:

This study was designed as a retrospective analysis of case records of patients with IE or suspected IE between June 2000 and July 2002 at Hospital Tengku Ampuan Afzan (HTAA), Kuantan. HTAA is a general hospital in the state of Pahang, Malaysia. It also serves as the

Keywords: Infective endocarditis, Intravenous drug use, Malaysia

teaching hospital for the medical faculty of the International Islamic University Malaysia. Its catchment area includes 4 referring hospitals namely Hospital Mentakab, Hospital Pekan, Hospital Kemaman, and Hospital Muazzam Shah. Sixty seven in-patients diagnosed as IE or suspected IE between June 2000 and July 2002 were identified from hospital records; 45 of whom fulfilled the clinical, microbiological, and echocardiographic criteria (Duke criteria) described by Durack et al[7] (1994) and were included in the present study. Data on the patients' demographic characteristics, medication received prior to admission, predisposing factors, clinical findings, complications, result of investigations, duration of hospital stay and clinical outcome were extracted from the case sheets.

Statistical analysis was done using SPSS version 10. Students t test was used to compare mean age and x^2 test was used to compare proportion among two different groups and a p value of <0.05 was taken as statistically significant.

RESULTS:

A total of 45 cases of IE were included in the study. The overall incidence was calculated to be approximately 10 cases/100,000 inhabitants / year. Majority of the patients (n= 41, 91.9%) were from Kuantan and the rest were referrals from Pekan (n=3) and Maran (n=1). Almost all were male (n=44) and their mean age was 31.9 years (range 18 - 57 years) as shown in Table 1. Thirty nine patients (86.7%) were intravenous drug users (IVDUs), 3 (6.7%) had rheumatic heart disease, 2 (4.4%) had mitral valve prolapse and one (2.2%) had congenital heart disease (ventricular septal defect). IVDU patients had a mean age of 30.74 ±7.39 years and were significantly younger (p= 0.017) than non–IVDU patients (mean age 39.5±11.82 years).

Table 2 summarizes the symptoms present at the time of admission. Fever was the commonest presenting complaint affecting 89.7% of IVDU and 83.3% of non-IVDU. Most patients (77.8%) presented with fever of less than 2 weeks duration. Fatigability was the second most common symptom which occurred in 82.2 % of all patients, followed by shortness of breath in 30 cases (66.7%) with associated cough in 26 cases (57.8%).

Table3 shows the microbiological and echocardiographic findings of our cases. Among IVDUs *Staphylococcus aureus* was the commonest organism (61.5%) followed by streptococci (17.9 %). All staphylococci isolated were methicillin-sensitive. Among patients who had positive cultures for streptococci, beta-haemolytic group G was the commonest (85.7%) followed by viridans streptococci (14.3%). Among non-IVDU, viridans streptococci were isolated in 2 cases (33.3%), enterococcus in 1 case (16.6%) and *Staphylococcus aureus* in one case (16.6%). Blood culture was negative in 9 patients (20%) of whom 7 had relapse and the other 2 had received antibiotics from general practitioners before admission.

Echocardiography results (Table 3) were available in 40 cases only. Among IVDU, the tricuspid valve alone was involved in 76.5% of cases. Involvement of more than one valve was found in 2 cases (5.1%). Among non-IVDUs, vegetations were on the mitral valve in 4 (66.6%) patients. No vegetations were found in 14.7% of IVDUs and 33.3% of non-IVDUs.

Table 4 shows the complications among the 45 cases studied. In our study there were no major complications in the non-IVDU group. Among IVDU patients, multiple lung abscesses were the commonest complication seen in 8 cases (20.5%) and 4 (10.3%) showed bronchopneumonia on chest X-ray. One IVDU patient presented with septic shock and died in the intensive care unit.

Hepatitis B and Hepatitis C serology were positive in 17.9% and 33.3% of IVDUs patients respectively. Five (12.8%) of these cases were positive for both Hepatitis B and Hepatitis C. HIV-positive IVDU patients were more likely to have positive serology for hepatitis B and hepatitis C.

Fifteen of our patients (38.5%) were HIV positive, all of whom were IVDU. There was no

TABLE 1.
Patient Characteristics: N: 45

	IVDU* (n=39)	Non-IVDU(n=6)
Sex		
Male	39(100%)	5(83.4%)
Female	0	1(16.6%)
Age(Years)	30.74±7.39	39.5±11.82
Ethnic group		
Malay	34(87.2%)	4(66.7%)
Chinese	5(12.8%)	2(33.3%)
Others	0	0
Predisposing disease		
Rheumatic Heart disease	0	3 (50%)
Mitral valve prolapse	0	2 (33.3%)
Congenital heart disease		1(16.7%)
IVDU	39 (100%)	0

*IVDU is intravenous drug user
**Age is expressed as mean and standard deviation

TA BLE 2.
Clinical Manifestations at the time of admission

Symptom	No	%
Fever	40	88.9
Duration <2 weeks	35	77.8
Duration >2 weeks	5	11.1
Fatigue	37	82.2
Breathlessness	30	66.7
Cough	26	57.8

TA BLE 3.

Comparison of microbiology and vegetation sites between IVDU and non-IVDU cases with IE

Culture	No n=45	Organism	IVDU n=39	%	Non IVDU n=6	%
Culture-positive	36	*S. Aureus*	24	61.5	1	16.6
		Streptococci	7	17.9	4	66.66
		- *Streptococcus viridans*	1		2	
		- Group G streptococci	6		0	
		- Enterococci	0		1	
		Others	0	0	1	16.6
Culture-negative	9		8	20.51	1	16.6

Vegetations*	Site	IVDU n=34	%	Non–IVDU n=6	%
	Tricuspid valve only	26	76.5	0	0
	Mitral valve only	1	2.94	4	66.6
	Mitral and tricuspid valves	1	2.94	0	0
	Aortic and tricuspid valves	1	2.94	0	0
	No vegetations detected	5	14.7	2	33.3

* Echocardiography report.

TABLE 4

Complications of 45 cases studied

Complications	IVDU (n=39) No	(%)	Non-IVDU (n=6) No	(%)
Multiple lung abscesses	8	20.5	0	0
Broncho pneumonia	4	10.25	0	0
Congestive cardiac failure	1	2.56	0	0
Renal Failure	1	2.56	0	0
Septic shock	1	2.56	0	0

TABLE 5

Comparison between HIV-positive and HIV negative IVDU cases with IE

	HIV positive (n=15)	(%)	HIV negative (n=24)	(%)	P value
Microbiology					
Staph Aureus	8	53.3	16	66.6	NS
Streptococcus	2	13.3	5	20.8	NS
Vegetation Site					
Tricuspid Valve	13	86.6	13	54.1	NS
Multiple Valves	0	0	1	4.16	NS
Hepatitis Serology					
Hepatitis B	6	40	1	4.16	$p<0.05$
Hepatitis C	8	53.3	5	20.8	$P<0.05$

statistically .significant difference in bacteriological and echocardiographic findings among HIV-positive and HIV-negative patients.

All patients received antibiotics for 4-8 weeks (mean 36 days) depending on complications with a success rate of 91%. Three IVDU patients took their own discharge and 1 patient died due to septic shock.

DISCUSSION:

IE continues to be a serious medical problem despite advances in diagnostic techniques and highly effective antibiotics. The estimated incidence of IE in our study was 10 cases per 100,000 per year. The high incidence may be related to IVDU as 86.7% of our patients were IVDUs. The incidence of IE among IVDU is believed to be 100 to 1000 times higher than in the general population.[10] Pathogens usually come from the skin and local infections at injection sites, contaminated needles, syringes, the drug itself, saliva or contaminated water used as a vehicle for drug administration. To the best of our knowledge, there is no previous study of IE in IVDUs among the local population. Limitations of the present study were that the data were collected from a state hospital and numbers were not large enough to allow definitive conclusions.

Infective endocarditis in IVDUs follows an acute course of 1-2 weeks among our patients. The outstanding feature was right-sided native valve endocarditis with involvement of the tricuspid valve alone in 76.5% of cases. This is in accordance with earlier studies.[11,12] Among IVDUs *Staphylococcus aureus* was the commonest organism (61.5%) followed by streptococci (17.9 %). Group G streptococci accounted for less than 1% of the total cases of IE in previous studies. In our study, they were isolated in 6 IVDU

patients (15.4%). Group G streptococci are part of the normal flora of skin, nasopharynx and gastrointestinal tract and have been reported among alcoholics and IVDUs. The portal of entry is the skin and the clinical presentation is often acute.[13] Right-sided native valve endocarditis in IVDUs is usually due to *Staphylococcus aureus* and is managed with 4 weeks of cloxacillin, although shorter 2-week courses of cloxacillin and gentamicin in combination may also suffice.[14,15,16] Our findings suggest that penicillin should be considered for IVDU patients with IE who do not respond to cloxacillin.

In many parts of the world IVDU is the major mode of HIV transmission due to the sharing of contaminated injecting equipment. According to a report by the Center for Harm Reduction in Australia's Burnet Institute drug use had become one of the major causes of the HIV epidemic in the Asia, based on an illicit drug and injection safety study of 20 Asian countries. All 15 of our HIV-positive patients, were IVDU. All responded to medical treatment and did not show any statistically significant difference in microbiology, echocardiography and outcome from HIV-negative cases. Our results are in agreement with earlier studies.[17] Ten of our patients had a previous history of IE out of which 7 had relapse, probably due to continuing intravenous illicit drug use. Faith and religious beliefs are among the most influential factors affecting human behavior. A recent review [18] concluded that there is strong evidence that religious or spiritual involvement is associated with decreased risk of substance abuse, and addicts are more likely to report a lack of religious affiliation.

Conclusion

Intravenous drug use has been the commonest predisposing factor for infective endocarditis among our patients. Intervention programmes for IVDUs have not been successful and a large number of patients continue to use narcotics. These programmes should be strengthened and better targeted to inculcate in the minds of vulnerable young people the dangers of narcotic drugs, and sharing injecting equipment. Morality and ethics has to be brought back into the picture and we probably have to change hearts through spiritual motivation. Further large-scale prospective studies are necessary to evaluate the efficacy of current short-course regimens for IE among IVDU.

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The Current Pattern of Surgically treated Thyroid diseases in the Medinah region of Saudi Arabia

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Abstract

The aim is to study the clinicopathological characteristics, the incidence of thyroid cancer and treatment results of surgically treated nodular thyroid disease in Medina region and their comparison with other series. Retrospective review of 189 surgically treated patients with thyroid disease at King Fahad hospital and Ohud Hospital Medinah Munawarah, Kingdom of Saudi Arabia was undertaken. Analysis of clinicopathologic characteristics, age correlation to different risk factors, incidence of malignancy and outcome of surgery was done and results were compared to the other reported studies from other regions inside and outside the Kingdom of Saudi Arabia. Total of 189 thyroidectomies (160 female and 29 males) were performed between April 2000 and July 2003 in two hospitals by the same surgical team. The peak frequency of goiter was in third and fourth decade of life. Female preponderance was seen in this study with female to male ratio of 5.5:1. Malignancy was found in 19.5% cases. Papillary carcinoma was the most common malignancy (91.8%) followed by follicular (5.4%) and medullary carcinoma (2.7%), male: female ratio for patients with thyroid malignancy was 1:2.7. Over all complication rate was 4.2%, the laryngeal nerve injury was low (1.5%). The pattern of thyroid diseases in Medinah Munawarah is generally similar to other regions of Saudi Arabia, with few regional variations. Fine needle aspiration and/or ultrasonography are important initial diagnostic aids in the solitary nodules and goiter. The surgery for toxic goiter is declining. Thyroid cancer is still one of the important endocrine cancers among females. Thyroidectomy with the controversy regarding its extent for thyroid diseases is a common procedure with an extremely low mortality. It is associated with specific morbidities which are related to the experience of the surgeon, however very low surgical morbidities rates for total thyroidectomy are reported in specialized centers. High incidence of malignancy in this region needs preventive efforts and further probe.

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INTRODUCTION.

Goiter occurs world wide and is the commonest cause of thyroid enlargement occurring in 3-5% of the population.[1,2] The large majority of them 70-90% are benign.[3] Patients with thyroid nodules are at a risk of 1.5% to 38.1% of cancer.[4] But overall incidence of thyroid malignancy is low. It accounts for 0.5 and 1.0 % of all cancers, and between 3.3% and 17% of all thyroid diseases.[5] In the Kingdom of Saudi Arabia collectively it accounts for 5.4% of the all newly diagnosed cancer cases.[6] Thyroid cancer is reported to be the second common cancer among Saudi women.[7] The best chance for cure is by total or near total thyroidectomy as an initial treatment in malignant cases.[8] The true pattern of thyroid swelling is still not known as only few controlled studies have been reported.[9-12] Present study was undertaken to evaluate the pattern of thyroid diseases treated surgically in Medina region of Kingdom Of Saudi Arabia.

PATIENTS AND METHODS:

During the period from April 2000-July 2003, 189 thyroidectomies were performed by the same surgical team at two main hospitals of Medinah Munawarh, King Fahad Hospital and Ohud hospital of the city of Medina. Patients were identified from the histopathological reports of all resected thyroid specimens. Resected specimens were reported by the histopathologist specially trained for thyroid disorders. The medical notes were reviewed for age, sex, nationality, family history of thyroid disease, clinical presentation, physical examination of neck included goiter and cervical lymph nodes. The data included all

Key words; *Thyroid; Goiter; Thyroidectomy; Medina; Saudi Arabia.*
Abbreviations; FNAC = Fine needle aspiration cytology KSA=Kingdom of Saudi Arabia; CT=Computerized axial tomography; MRI=Magnetic resonance imaging

preoperative investigations, thyroid function test, thyroid ultrasonography scan which was done routinely in most of the patients to confirm the solitary nature of nodule or not. All these patients had fine needle aspiration cytology done at histopathology department of King Fahad hospital Medina. The decision to operate was made on clinical and laboratory findings. The indications for surgery in these patients followed accepted practice i.e. suspicion of malignancy in rapid enlargement of a goiter, the presence of compression effects or the cosmetic reasons. In the toxic group surgery was the preferred treatment after failed medical treatment or non compliance with the antithyroid therapy. Patients were prepared for thyroid surgery and general anesthesia .All routine and special blood tests like thyroid antibodies, thyroid function tests were done from the outpatient clinic. Patients with clinically palpable solitary nodules were subjected to ultrasonography to exclude multinodularity. Computerized tomography scan was done in some cases of papillary carcinoma to detect non-palpable lymph node metastases or invasion of thyroid gland into surrounding structures. Patients having associated medical problems like asthma, diabetes and hypertension would be admitted two days before to make them fit for surgery and general anesthesia. Frozen section would be done in patients suspicious of metastases in cervical lymph nodes after making prior arrangement with histopathological department.

Table1
Age and sex of patients

Age group	Male Number	Female Number	Total patients
<20 years	3	23	26
21-30	8	55	63
31-40	6	44	50
41-50	3	25	28
51-60	5	9	14
>61	4	4	8
Total	**29**	**160**	**189**
(%)	(15.35)	(84.05)	(100)

RESULTS;

The peak frequency of goiter was in third and fourth decades .The youngest patient in our series was 12 years male with nodular goiter. The age ranged from 12 –90years. Females constituted 85% of this series, and the female to male ratio was 5.5:1. Women accounted for 83 cases (89.2%) of the simple goiter and 43 cases (84.3%) of adenomas, which were mostly follicular except in one of Hurthle cell type.The relative incidence of thyroid pathology is shown in tableII.

93 patients (49.2%) had simple goiter. Non- toxic adenomas were 51 and out of which the majority were follicular, two patients had Hurthle cell tumors and cystic goiter was found in 15 patients. Of the 3 patient with thyroiditis, two patients had autoimmune(Hashimoto's disease) and one was granulomatous thyroiditis.Thyroid malignancy was found in 37 cases(19.5%).Our histological typing of cancer as shown in table III is as per the classification proposed by the WHO in Geneva in 1974.[13]

Table II: Distribution of the types of goiter; Number=189

Characteristics	Number of patients	Percentage (%)
Simple goiter	93	49.2
Malignant Goiter	37	19.5
Adenoma	51	37.0
Toxic	2	1.1
Thyroiditis	3	1.6
*Others	3	1.6
**Thyroglossalcyst(2),		
Total	189	

Table III: Histopathological types of cancer thyroid

Histopathological Type	Male Number (%)	Female Number (%)	Total Number (%)
Papillary	10(29.5)	24(70.5)	34(91.8%)
Follicular	0(0)	2(100.0)	2(5.5%)
Medullary	0(0)	1(100.0)	1(2.7%)
Anaplastic	0(0)	0(0)	0(0)
Total	**10(27)**	**27(73)**	**37(100)**

Papillary carcinoma was the most common ((91.8%) malignancy of thyroid followed by follicular (5.4%) and Medullary carcinoma (2.7%), with papillary to follicular carcinoma ratio of 17:1. The male to female ratio for patients with thyroid malignancy in this series is almost 1:2 as is shown in table IV.No malignant goiters were found in patients younger than 12years.

The post operative complications we encountered in present series is shown in tableV

DISCUSSION;

Until the late 1800s, surgical treatment of thyroid disorders was reserved for patients with impending death from suffocation because of the fear of surgical complications, such as hemorrhage and infection. Today thyroidectomy is a routine procedure because of the introduction of safe anesthesia, antisepsis, fine surgical instruments and development of new techniques, offering the chance of cure to many patients.[3,14]. Overall death from thyroid surgery is rare, and the incidence of complications like recurrent laryngeal nerve injury, neck hematoma,

thyroid storm and hypoaparathyroidism is low.[15] Despite advances in the management of thyroid diseases the ideal

TableIV: Age and Sex distribution of all carcinoma of thyroid patients

Age (years)	Total number.	Male number	Female number.
<20years	5	2	3
21-30	8	1	7
31-40	10	1	9
41-50	6	1	5
51-60	3	2	1
>61	5	3	2
Total (percentage)	37(100)	10(27%)	27(73%)

surgical treatment however, remains a controversy amongst various thyroid surgeons. A major reason is differences in experience and attitudes towards surgical

TableV: Complications of Thyroidectomies; 8/189

Complications	Number.	Percentage
Hemorrhage	1	0.52%
Huskiness(temporary)	2	1.05%
Hypocalcaemia Temporary.	3	1.5%
Wound infection	1	0.52%
Hypertrophied scar	1	0.52%
Total.	8	4.2%

resection of benign and malignant thyroid lesions and the possibility of complications.[16-18] The first true extirpation of the thyroid was performed in the year 330 by Albucasis ,an Arab court physician living in Baghdad.[19] In 1868 ,William Warren Green of Portland performed the successful thyroidectomy.[20] Theodor Kocher became the first surgeon to win Nobel prize in Medicine for his outstanding contributions to the understanding of thyroid disease and perfecting the technique of thyroidectomy[17] by then the overall mortality had decreased from 50.0% to 4.5%.[21] Since Kocher's time there have been considerable advances in the understanding of thyroid disorders and in the effective management of patients with thyroid nodules. Numerous controversies, however, regarding the preoperative evaluation and extent of thyroidectomy in the management of differentiated carcinoma still remains[17]. This may partly be due to lack of uniformly accepted management protocol between different surgeons and hospitals.[23] The true pattern of goiters in Saudi Arabia is not yet clear due to widely environmental and geographical conditions with different social habits[9-12] Present study with above background was attempted to represent a general overview of surgically treated thyroid diseases in the Medina city and then comparing the pattern of observed benign and malignant diseases with other parts of Kingdom.

Simple goiter is the commonest pathology found in the thyroid gland in endemic area and accounts for more than 70% of thyroid swellings.[23] In the present series simple goiter was commonest and accounted for 93 cases (9.2%). The frequency of multinodular goiter in our study is one of the highest as compared to other studies from Saudi Arabia and other parts of world except the one reported from Jeddah by Nasr et al[9] Autoimmune thyroiditis (Hashimoto's disease) has variable geographic distribution and is said to be rare amongst Africans,[24] but it is a common cause of diffuse thyroid

Table VI:Comparison of Thyroid diseases with other reported studies from Saudi Arabia and neighboring countries.

Country/Region	Author	Number	MN%	Adenoma	Toxic	Auto	Malig
KSA/Medina	Bouq(current)	189	49.2%	27%	1.1%	1.6%	19.5%
KSA/Riyadh	Kona et al[11]	172	38.4%	12.2%	9.9%	9.3%	25.4%
KSA/Riyadh	Mofti et al[13]	158	31%	30%	5%	3%	29%
KSA/Riyadh	Tammem[14]	380	28.1%	27.3%	14.7%	6.6%	21.3%
KSA/Jeddah	Nasr[9]		60%	8.7%	10.2%	-	14.5%
KSA/Asir	Abu-eshy[10]	361	43.7%	24.6%	7.7%	6.4%	13%
KSA/Bisha	Ghamady[12]	100	31%	29%	7%	11%	14%
Yemen	Hureibi[25]	282	33.7%	49%	10.5%	-	3.9%
Ethopia	Menigstu[26]	373	22.3%	23.6%	43.7%	1.2%	0.3%
Libya	Elhamel[27]	618	44.5%	32.5%	9.5%	3.7%	9.7%

***KSA=Kingdom of Saudi Arabia; MN=Multinodular goiter Toxic= Toxic goiter Auto=Autoimmune thyroiditis**

enlargement in parts of United states of America[23,25] The incidence of toxic goiter(1.1%) was fairly low as compared to other studies of Saudi Arabia. The possible reason that surgery for toxic goiters are decreasing these days is because of growing public awareness, and better primary health care facilities in Saudi Arabia. The opening of specialized endocrinology clinics throughout the Kingdom has also contributed in better management of thyroid diseases. Thus surgery is restricted to patients who are referred to surgery by endocrinologist either because of non compliance or those who do not respond to conservative treatment. This observation may reflect a healthy trend in this Arab society regarding patient compliance due to health education of general population by media and improvement in primary health care. The reported incidence of malignancy in surgically treated goiters varies widely from 2.3 to 27% from one geographical area to another.[26] In our series, the proportion of patients with cancer is high 19.5% as is shown in table II and VI .But this high incidence is not statistically significant when compared to different regions of Saudi Arabia whereas it is highly significant as compared to some studies done in many other geographical areas outside Saudi Arabia as shown in table II and VI.The implication of this study ,which suggests that one in five patients with thyroid swelling has a malignant goiter, needs verification by further studies, preferably in a large population of patients to minimize bias. The primary factor behind this apparently high incidence of thyroid cancer in this area is not known. Several etiological factors including accidental irradiation of head and neck during childhood and young adulthood have been postulated predisposing to the development of differentiated thyroid carcinomas, and most of these are of papillary type.[27-30] In the health conscious world of present times, diagnostic radiation exposure in childhood is so common as majority of the patients involved in present study had an exposure to radiation .No known etiological factors(radiation exposure, endemic goiter, cancer thyroid among family) could be confirmed in any of these patients in this study. Ultrasound is more sensitive than either palpation or thyroid radionuclide scanning in detecting structural abnormalities in irradiated individuals. Both lobes of the gland and adjacent neck structures are examined, and normal features and any abnormalities are characterized with respect to size, shape, echogenicity, echostructure and other sonographic features. Ultrasonography of the neck region is also a valuable tool for measuring the progress of therapy, detecting non palpable or questionably palpable thyroid nodules and differentiating solid from cystic nodules.[31] This non invasive tool was very helpful in examining our female patients with socio religious restrictions to expose fully the region of neck.Ultrasonography, however, has no role as a screening test for evaluating patients with thyroid nodules for malignancy. If fine needle aspiration cytology is used in conjunction with ultrasonography, it is helpful for documenting adjacent lymhadenopathy besides the nature, size and number of thyroid nodules. Ultrasonography was used as an additional tool in present study to document thyroid nodule size in three dimensions for patients being followed nonoperatively and for evaluation of the presence or changes in cervical lymphadenopathy and also post operatively for recurrence of disease.

With some exceptions Computed tomography (CT) or Magnetic resonance imaging(MRI) is usually unnecessary for evaluation of thyroid lesions.[32] However in present series CT scan was used for the patients as is recommended with large invasive or substernal lesions in which the limits of the tumors were difficult to determine. Magnetic resonance imaging has been reported to be more valuable than CT scan for differentiating between recurrent or persistent tumor and post operative fibrosis,[33] in the present series MRI was not used for any patient as its need was not felt. During the past decade, FNAC has become a widely accepted diagnostic test for the initial preoperative assessment of patients [34,35] and has clearly decreased the number of unnecessary thyroid operations.[36] The reported accuracy of FNAC ranges from 70% to 97%.[37]The false positive rates of FNAC generally range from 0.3 to 9% whereas the false negative rates ranges from 0% to 4%.[38]All our patients had FNAC before surgery. The accuracy of FNAC, false positive was 0.5%, false negative rate was 2.1% which is comparable to any international standards. Even though FNAC is considered the diagnostic test of choice for most patients with thyroid nodules, it also has some limitations [39],sometimes leading to reoperative neck exploration and completion thyroidectomy in patients with a missed diagnosis of malignancy and thus supports the limited usefulness of frozen section examination in selected patients to confirm the diagnosis of malignancy. Frozen section does have a role if diagnosis by FNAC is controversial or inconclusive. It is also useful for the investigation of enlarged or suspicious cervical lymph nodes and other suspected nodules found during surgery.[40]We performed frozen section studies only in few doubtful cases of papillary carcinoma with suspected spread to adjacent cervical lymph nodes. In the present study papillary carcinoma was the commonest malignancy observed (91.8%) and it was higher as compared to the other studies from Kingdom as is shown in table VII.

The incidence of papillary carcinoma seen in our cases is almost the same as seen in some studies done in Europe[41], whereas it was low (50-89%) in another study from Europe[42] as compared to the present study. The malignant thyroid diseases as seen in table III and VII were of only three type's i.e. papillary carcinoma (91.8%), follicular carcinoma (5.4%) and medullary carcinoma (2.7%).The incidence of medullary carcinoma is less than 1% in most of the studies mentioned above. No anaplastic, lymphoma or Hurthle cell carcinoma was

found in our study. These results are different from the study done recently at Bisha, a high altitude area of Saudi Arabia, where no case of follicular, medullary or anaplastic carcinoma and lymphomas were found.[43] These authors explained that follicular carcinoma has reduced in their region partly due to the recently observed increase in dietary intake of iodine by the local population. As seen in tableVI and mentioned before the incidence of malignancy (19.5%) is higher in our study as compared to reports from Libya 9.7%, Yemen 3.9%, Ethopia 3% ,USA 5.8% and South Africa 5.4%.[5,44,45] While comparing different studies from the Kingdom a variable incidence regarding malignancy was observed; Jeddah(Nasr)14.5%, Riyadh (Al-Tammem)21.3%,Riyadh(Mofti et al)29.0% and Asir(Abu-eshy) 13.0% Bisha (Ghamady)14% [9,11,12,42,43] This variation although statistically not significant with these number of patients ,it needs further evaluation whether local environmental factors or social habits are playing any role.

But a recent study done by Abdulmughni [49] from Yemen has quoted almost similar figures to our study. Patients with thyroid carcinoma in his study comprised 17.7% of goiter patients. Females constituted 89.7% and males 10.3%. Multinodular swelling was the most common clinical finding (43.3%), papillary carcinoma accounted for 93.8% of the cases. The papillary/follicular carcinoma ratio was 22:1. According to the author salt iodization program might have an effect on the incidence of thyroid malignancy, and on the papillary/follicular carcinoma ratio.[49]

As shown in table VII the ratio of papillary to follicular in the earlier published studies like those of Elhamel[5], Tammem [11], Mofti [12] and Hurebi [45] is very low. Similarly the incidence of papillary carcinoma is low and that of follicular is high as compared to the studies like that of Abu-eshy[44] done later. In our study and that done by Abdulmughni the percentage of papillary and the ratio between the papillary and follicular is high[49] It looks that during the era of uniodized salt the number of cases with papillary variety were low and they were well compensated by follicular variety which has been reversed with the use of iodized salt. The shift of pathology varieties have been toward papillary. The number of follicular cancer has been much reduced in these areas and places where this salt is the main or the only salt in the diet. Many other factors have been postulated for the increased incidence of papillary as compared to other varieties like closeness to sea with volcanic activity or chronic elevation of thyroid stimulating hormones[50]. But the possibility of this to happen at such a high level due to these factors that the shift in malignant varieties will be clearly seen is difficult to understand in our cases.

Most of the studies have not mentioned the complications they faced our complication rate was low and comparable to the other studies as the majority of the operations were done by a single experienced surgeon.

Conclusion;

Saudi Arabia is a vast country occupying most of the Arabian Peninsula with widely environmental and geographical conditions .Marked variations in the relative frequency of diseases in different regions are recognized .There is a lot of controversy regarding thyroid investigations and management of thyroid disorders especially with the extent of resection in differentiated carcinomas. An experienced thyroid surgeon can treat patients with thyroid diseases with minimal complications. More extensive initial surgery such as total or near total thyroidectomy seems to decrease tumor recurrence and prolong life. We believe total or near total thyroidectomy is the treatment of choice even for benign thyroid diseases because even low-risk patients have a 4% or 5% risk of eventually dying of thyroid cancer [37].If the risk of death from thyroid cancer can be decreased to 1% or 2% and the rate of serious complications to 1% or 2%, the authors believe total thyroidectomy is indicated. Most of these patients can be discharged within 1 day of total thyroidectomy.Use of FNAC for the preoperative assessment of patients with thyroid nodules has resulted in increase in the yield of thyroid carcinoma at operation, and FNAC has become the single most important initial diagnostic test. FNAC however continues to have some limitations when used as the sole preoperative diagnostic test and should never overrule good clinical judgment. There is need to have more detailed controlled studies regarding the pattern of diseases admitted and surgically treated at tertiary healthcare facilities in Saudi Arabia, so that appropriate uniform intervention policy could be planned.

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Lithium therapeutic drug monitoring pattern at a tertiary care hospital in India

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Abstract

Therapeutic drug monitoring (TDM), a comparatively new investigational procedure in Clinical Pharmacology, is considered useful in patients suffering from mood disorders though it increases the health care cost. The aim of this study was to evaluate the pattern of TDM of Lithium in a tertiary care center and compare this with other centers.From the archived data bank, estimated level of lithium were noted down, tabulated and compared over the period of six years (1997-2003). Total 10,143 samples were analyzed over the six years, values were found normal in 8,451 (83.32%), low in 804 (7.92%) and toxic in 888 (8.75%). No difference was observed with respect to sex. This study indicates a pattern of increasing awareness and caution among physicians who prescribe lithium. The absence of a difference in plasma lithium levels with respect to sex is a finding that is dissimilar to the observations in other centers. TDM assisted management of psychiatric patients is useful for early detection of ADR and to prevent lack of therapeutic response.

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Introduction

Despite the availability of numerous drugs, lithium remains the drug of choice for bipolar disorder. Due to its narrow therapeutic index, the margin between toxic, therapeutic and sub-therapeutic serum levels are liable to be crossed. Individual variation, poor compliance, renal disease, seasonal variation etc are some reasons which make plasma lithium level estimation important.[1,2] The aim of the current study was to evaluate the pattern of therapeutic drug monitoring (TDM) of lithium and to compare this with other centers.

Methods

This study was conducted in the Departments of Pharmacology and Psychiatry, PGIMER, Chandigarh. Records were obtained of blood samples received and analyzed from 1997 to 2003 from archived databank. Plasma levels of lithium <0.35, 0.35-1 and >1 meq/L were considered sub-therapeutic (low), therapeutic (normal) and toxic (high) respectively. The trend of plasma lithium levels was calculated as percentage of patients in each of the three categories over the six year period.

TDM of Lithium was done using 654 Na/K/Li ion Selective Electrode Analyzer (ISE). The blood sample was centrifuged at 3000 rpm for 15 min for plasma separation and placed in the analyzer. Detection was based on the change in electrical potential relative to standard lithium electrodes placed within the analyzer. These values have shown to correlate with flame photometry levels.

Results

Among the 10,143 samples analyzed over the six years values were normal in 8,451 (83.32%), low in 804 (7.92%) and toxic in 888 (8.75%) (Table.1). There was increasing trend for low values and decreasing trend for normal values observed over the 6 years (Figure.1). There was no difference observed when analysis was done with respect to sex.

Discussion

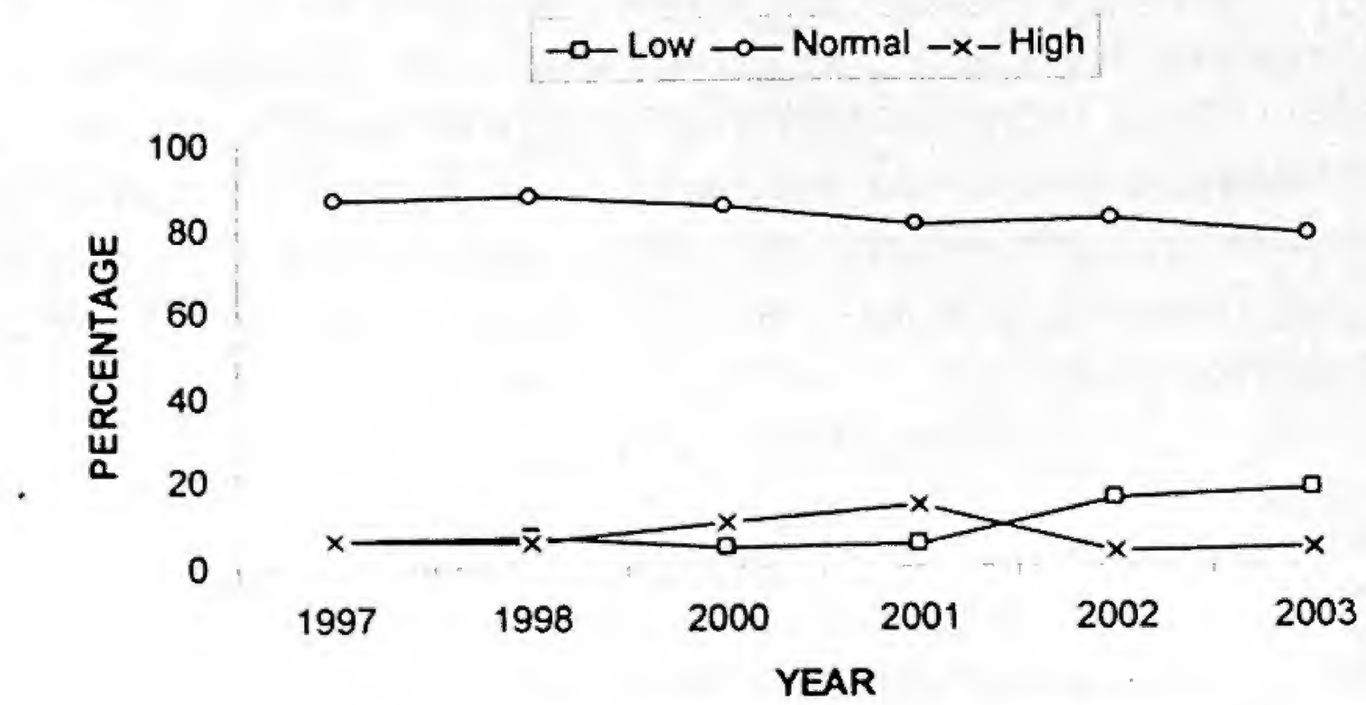
Analysis showed 83.32% of samples in normal range and 16.67% in the abnormal range. Patients with abnormal values had low

Key words: TDM, lithium, toxicity, pattern

Table 1. Number of lithium estimations showing values in normal, low and high ranges

Year of data collection	Low	Normal	High	Total
1997	114	1482	106	1702
1998	68	863	57	988
2000	107	1988	238	2333
2001	142	2251	410	2803
2002	252	1336	49	1637
2003	121	531	28	680
Total number of estimations in each group	804	8451	888	10143

Fig. 1. Percentage of normal, low and high lithium values over the six years.



levels (7.92%) and higher levels (8.75%) over the period of six years. Increased awareness of the clinicians regarding toxicity and lack of therapeutic response seems to be the reason for this change. Other studies have shown 6.8% of patients in the toxic range[3] and 50% having low levels of plasma lithium[4] However, only 27.8% of patients with excessive levels had signs and symptoms of toxicity and women were significantly more likely to have higher plasma levels.[3] Contrary to these findings, our study did not show any difference in plasma lithium levels when compared for gender i.e. there was no predisposition to lithium toxicity for either males or females.

The international standard for normal therapeutic range of lithium is 0.6 – 1.2 meq/L. In our study different values for subtherapeutic, therapeutic and toxic range are used based on earlier studies showing clinical correlation of such a categorization in our institute. Coefficient of variation of our Na/K/Li analyzer was 1-2% which is in the acceptable range.[5]

At the therapeutically effective limits, lithium increases urine output and decreases creatinine clearance in men with decrease in renal concentrating ability and can alter calcium homeostasis. Non-compliance with lithium therapy can lead to relapse of the patient. It shows genetic variability in pharmacokinetics, drug-drug interactions, and high levels can lead to adverse effects like long term neurotoxicity following poisoning.[6,7,8] Patients with nephrogenic diabetes insipidus, older age, abnormal thyroid function and impaired renal function are susceptible to toxicity. This drug has its hazards in pregnancy leading to increased rates of cardiovascular malformations and perinatal death.[9] This stresses the need of therapeutic drug monitoring of lithium. Unfortunately, use of TDM often follows an "all or none" pattern by clinicians, i.e. there may be repeated monitoring when not required or lack of TDM in other situations.[11]

Therapeutic drug monitoring using salivary lithium as an index to plasma levels has been tried but is not accepted as a valid tool due to wide individual variations following precipitation by ionic content of saliva, adrenocortical and psychosomatic influences, and effect of psychotropic drugs on saliva production, etc.[12]

Evidence from this study indicates a pattern of increasing awareness and caution when using a drug of narrow therapeutic range like lithium. TDM for lithium definitely places an additional economic burden on the patient as well as health care providers. TDM-assisted psychiatric treatment is potentially useful and cost-effective in decreasing the ADR and preventing lack of response.[13]

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Original Article

Guidelines for Removal of Foreign Bodies In Pediatric Airway

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Abstract

A retrospective study of 74 cases of tracheobronchial foreign bodies was analyzed. Clinical, radiological features, types & location of foreign bodies were studied. Of the 74 children who underwent rigid bronchoscopy, 70 had tracheobronchial foreign bodies. History of choking was elicited in 90% of cases, 77% of children were below the age of 3 years. Twenty patients (31.1%) reported within 24 hrs of the event. There was a delay of more than 2 weeks in 11 (15%) cases. Vegetative foreign body, mainly peanuts were commonly present. In many cases referral was delayed as the diagnosis was missed initially. Stress is laid on proper instrumentation, through training and teamwork to achieve goal of zero mortality and no major complication.

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INTRODUCTION

Foreign body aspiration is a common problem in children, and the most common cause of accidental death, at home in children under six years of age[1,2]. It is estimated that almost 600 children under 15 years of age die per year in U.S.A. following aspiration of foreign bodies[3].

Paediatric bronchoscopy for the removal of foreign bodies is the most challenging task both for the E.N.T. specialist and the anaesthesiologist. Many years ago, in the absence of sensitive monitors, good anaesthesia machines and lack of ventilating bronchoscopes, bronchoscopy was often an unpleasant experience for the endoscopist, anaesthesiologist and the patient, fraught with very high morality and morbidity. Over the years, with better availability of good equipment, the scenario has changed. Avoidance of hazards demands the optimum in skills, communication and teamwork of the E.N.T. specialist and anaesthesiologist. Most reports from both large and small series of foreign body removal from peadiatric airway include at least one death, while aspiration pneumonitis, consolidation and laryngeal oedema do occur in small percentage of cases[4-6] The challenge today is to avoid mortality at any cost and ways to overcome this are outlined in this original article.

MATERIAL & METHODS

This is a retrospective study of foreign body inhalation in children at Satish Mehta Clinic And Research Centre Pvt. Ltd., Jammu. We reviewed the records of 74 pediatric patients admitted between April 1999 to March 2005 with the diagnosis of foreign body Inhalation. The following data was collected: sex, age, residence, duration of illness, availability of definite history, need for tracheostomy, bronchoscopy findings, duration of hospital stay after its removal and complications. All patients suspected of foreign body aspiration were subjected to rigid bronchoscopy under general anaesthesia with controlled ventilation, using karlstorz pediatric ventilating bronchoscope.

RESULTS

Seventy four children were admitted with suspected foreign body aspiration during this period. No foreign body was found in 4 subjects and they were excluded from the analysis. Of 70 subjects with foreign body aspiration, 48 (68.5%) were boys and 22 (31.5%) were girls. Most patients (77%) were below 3 years of age, the median age of was 2.5 years (range 2 to 9 years). An equal number of children came from urban and rural communities. Twenty patients (31.4%) reported within the 24 hours of the

KEYWORDS: *Foreign body, Rigid bronchoscopy, tracheobronchial aspiration.*

event. The median duration of symptoms prior to admission was 72 hours. There was a delay of more than 2 weeks in 11 (15%). A definitive history of choking following foreign body aspiration was present in 63 (90%) cases.

Chief clinical features included:

History of choking (90%), History of paroxysmal cough (81.1%), History of fast breathing (81.1%), History of stridor (71%), decreased air entry (67%), wheezing (50%), fever (29%), cyanotic episodes (11%).

The number of patients were more every year in the month of January due to Lohri festival when peanuts are consumed in plenty in every house in Northern India.

Peanut was the commonest foreign body seen in 50 cases (71%), While other foreign bodies were almonds, cashew nuts, chunks of melon, carrot and plastic toys.

Chest radiographs were helpful in providing evidence of possible foreign body aspiration in 49 patients (70%). Radiological features of air trapping were seen in 44 (62.8%) cases, while collapse/ atelectasis was seen in 35 (50%) cases. Mediastinal shift was seen in 10% cases while a radio-opaque foreign body was evident in 3 cases (4.2%). Normal radiograph or one showing non specific findings was present in 30%. Details of treatment received prior to referral were available in 50 cases. The treatment received included antibiotics, intravenous fluids, oxygen supplementation and bronchodilators. Flexible bronchoscopy had been performed and presence of a foreign body confirmed in 6 cases from chest diseases hospital. One patient presented with mediastinal emphysema and surgical emphysema over neck and chest. After 1 week of conservative/ supportive medical treatment, once the emphysema completely disappeared, the child was taken up for rigid bronchoscopy.

Bronchoscopy showed tracheo-bronchial oedema or granulation tissue (50%), inflammation (40%) and purulent secretions in 15% cases. A single foreign body was present in 70% cases while multiple (two) in 20%, three in 10% and five in one case. In 70% of cases foreign body was lodged in right main bronchus, 20% in left main bronchus, 5% in sub glottis.

The foreign body was vegetative in most (61 cases) and inorganic in 9 cases. A check bronchoscopy was performed in all the cases in the same sitting to look for multiple or remnant foreign bodies. In 3 cases there was fragmentation of foreign body during removal and all fragments were removed in the same sitting. Majority of patients 90% were discharged the same day, while 7 patients (10%) stayed in the hospital for more than 2 days because of complication like fever, bronchospasm, poor nutrition and toxicity. Not a single mortality occurred due to team work of all the members which included one E.N.T. surgeon, two anesthetists, one pediatrician, one cardiothoracic surgeon on call and four paramedical staff members. The monitoring included E.C.G., heart rate, N.I.B.P., SpO_2 and end tidal CO_2.

DISCUSSION

While aspiration of foreign bodies into the tracheobronchial tree occurs in all age groups, infants and small children suffer most commonly. The anatomic relation of larynx, shouting, crying and playing while eating and lack of parental supervision contributes to this hazard. Most patients in this study were below 3 years of age, which is similar to that reported in other series[1].

The natural urge to explore the objects by mouth, lack of molar teeth to crush nuts and lack of supervision by parents may result in inhalation of foreign bodies in this age group.

The fact that about 15% of the patients arrived at the hospital more than 2 weeks after inhalation is of concern, bearing in mind that a positive history of aspiration was obtained in 90% patients. Some of the patients were treated before referral, with antibiotics and bronchodilators, before suspecting a foreign body. In patients who had been referred more than 7days after onset of symptoms, medical staff had often ignored the event of choking when the initial assessment was made. Factors, which may delay the diagnosis, include:-

a) Parental negligence and wrong diagnosis by the doctor.

b) Lack of symptoms, particularly after acute initial phase of dyspnoea.

c) Diverse clinical features due to inhalation of foreign body.

Common clinical features included choking, (90%) paroxysmal cough and fast breathing followed by stridor and decreased air entry. The classical triad of wheezing, paroxysmal cough and decreased air entry, considered highly suggestive of foreign bodies was seen in 35% of our cases as compared to 39% in other study[10].

Chest radiography is an important investigation for diagnosis, though fluoroscopy being a dynamic modality can be useful when chest skiagram in inspiratory phase is inconclusive. Since most foreign bodies are vegetative and thus radiolucent, their presence is usually established by the indirect signs of atelectasis or air trapping due to partial obstruction. In infants and very small children who may not be able to co-operate, assisted expiratory technique using pressure over the patient's epigastrium, applied during maximal exhalation, will result in a radiograph that is sensitive indicator of air trapping.

Vegetative foreign bodies are more dangerous as they swell up with bronchial secretions causing increased obstruction. They can also cause allergic and chemical bronchitis (vegetative bronchitis). This chemical bronchitis is more pronounced in peanuts due to release of its oil.

Multiple foreign bodies were seen in a high percentage of patients in the present study (28.1) as compared to 9-11% in previous studies[6].

Considering that most common culprit was the innocuous peanut, we feel a large number of these cases

could have been avoided if the parents, family and the health care providers were sensitized to the hazards of exposing small children below 3 years of age to nuts and certain small parts in the toys.

It is worth mentioning that most of series however large or small, included at least 1 or 2 deaths in attempts to remove tracheobronchial foreign body. In the present study we took all precautions and extra care so as to avoid this unpleasant experience. Following are the most crucial points in order to safe guard patients from mortality event.

SPECIAL CONSIDERATION IN BRONCHOSCOPY

A) Difficulty may be encountered in introducing bronchoscope especially for beginners. It is better to use laryngoscope in left hand to lift tongue so as to have a complete view of laryngeal inlet and then introduce bronchoscope with the right hand.

Beginners may find even this technique difficult. For them it is better if anaesthetist is asked to put endotracheal tube and then endoscopist follows the endotracheal tube till he/she reaches glottis when endotracheal tube is withdrawn and bronchoscope advanced after complete withdrawal of endotracheal tube. Pediatric larynx is very small, soft and mobile, taking help of anaesthetist should not be a matter of ego for endoscopist. At times one can ask the anaesthetist to put bronchoscope till trachea and then hand it over to you, as anaesthetist's job is to do intubation of airway daily hence their familiarity of airway is much more.

B) Another difficult situation in bronchoscopy of very small child (age 9 months to 18 months) is that the diameter of bronchus is small. Once you put suction tip or foreign body forceps vision is not possible. Two important steps worth mentioning here are:-

(i) Keep foreign body exactly in the centre of bronchoscopic view.

(ii) Open foreign body forceps just proximal to foreign body and your fingers shall be so trained, so as to act as eyes, that is tactile sensation should guide you whether you are holding foreign body or not.

C) Loose foreign body in trachea is difficult and dangerous, as with each air current from the bag, it can move up and down. For such a foreign body avoid neuromuscular blockade and maintain spontaneous ventilation. If not feasible better push the foreign body down to one bronchus where it gets lodged and then it becomes easy to grip the foreign body.

D) Another difficult situation is impacted vegetative foreign body with exuberant granulation around the foreign body. In such a situation one must use adrenaline soaked pledgets to decongest the area and then try to delineate the foreign body.

Next step is to dis-impact the foreign body so that a little space is created for the forceps to catch hold of foreign body. If it bleeds too much better not to fiddle and leave the foreign body as such. Give a course of broad spectrum antibiotics and steroids for 3 days to reduce active infection and oedema and try again. If difficulty is still encountered again better option is to accept defeat and let it be removed as a planned thoracotomy, rather than you causing bronchial/lung parenchymal injury and jeopardizing the child's life and health.

E) Another difficult situation is exceeding the limit for bronchoscopy and child is desaturating again and again. In such a situation it is better to withdraw bronchoscope and abandon the procedure. Patient should be given broad spectrum antibiotics and steroids to improve general condition of the child and then repeat the procedure after making proper assessment of general condition. A bed in pediatric ICU must be kept vacant for such cases.

F) An old long standing vegetative foreign body can become macerated and in this one has to clear the bronchus by repeated bronchoscopies (may be 4-5 times) and at times irrigation with saline and repeated suction may be essential to clear the muck and debris of foreign body.

G) After removal of foreign body from bronchus one must do 2nd look bronchoscopy so as to look for 2nd or multiple foreign bodies. Even at times part of foreign body may be left, which will be diagnosed and caught in 2nd look bronchoscopy.

Another important points is that always consult the anaesthetist and the pediatrician, who have seen patient preoperatively, to let you know about the improvement in air entry on the involved side after removal of foreign body. If anaesthetist or pediatrician says improvement is nil do check bronchoscopy and look for 2nd foreign body.

The judgment on airway improvement by another independent clinician leaves no chance of subjective error by the surgeon.

H) Sometimes you can get a patient with foreign body in the form of a cap of a pen with rounded surface facing the endoscopist. It is a difficult situation, as such you try to grip foreign body it slips and gets deeply impacted. The best thing in such a case is to use laser (yag), Radio frequency laser, or diathermy to make a hole/pit in the centre then grip it with forceps for removal. Same thing can be done for plastic gun pellet, by making two small pits as making hole in a solid body will take a long time.

Other solution for such foreign bodies is to get two skin hooks welded end on, after removing

the hook of proximal skin hook. The hook of 2nd skin hook can be easily negotiated beyond the foreign body and then rotate it by 90° to engage around foreign body or cap of pen and try to disimpact and move it towards trachea.

The author has faced all these situations and thus devised simple cost effective methods which can be made available at every centre. The author has rich experience of removal of foreign bodies in more than 200 cases over a period of 15 years, though in this study 70 cases with complete data are presented.

COMPLICATIONS

There is hardly any chance of complications if surgeon is meticulous, competent and equipment is of high quality with all emergency drugs available. It has been my practice to always call two competent anaesthetists, one takes care of I/V line and drugs while 2- takes care of airway/ventilation. So, the surgeon is completely focused on to endoscopic job. Always listen to anaesthetist's request of withdrawing bronchoscope or abandoning the procedure in case of desaturation or cardiac arrhythmias. Stablize the patient and repeat bronchoscopy after 48-72 hrs or refer for thoracotomy. The pediatrician is around for pre and postoperative treatment.

Surgeon should have an assistant to handover instrument and anaesthetist should have an assistant to load drugs. One more assistant is there in operation theatre as an extra help.

This makes a complete team and I don't think after these pre-requisities are met there is chance of any complication.

INTRAOPERATIVE COMPLICATIONS WITH REMEDIES

A) Injury to lips, epiglottis, vocal cords, trachea, carina and bronchial walls from inexperienced hands is a possibility. Proper training is the only remedy.

B) Hypoxia and cardiac arrest were complications of the past when ventilating bronchoscopes were not used for rigid endoscopy.

C) Inability to ventilate child due to anaesthetic circuit problem. Always do dummy practice before taking the patient in.

D) Laryngeal or subglottic oedema due to oversize bronchoscope or excessive manipulation can occur if the surgeon is a beginner.

E) Subglottic impaction of foreign body can occur. The remedy is always remove foreign body from posterior part of glottis, as it is wide.

F) Sometimes foreign body may get lost after you have negotiated it through glottis. Always remember to search nasopharynx in such cases.

POSTOPERATIVE PROBLEMS

1) **Laryngospasm:** This is due to the secretions irritating supraglottis, as a result vocal cords get adducted. Children are more prone to laryngospasm than adults.

Laryngospasm is more common in winters than summers. Rich supply of supraglottis with nerve plexuses of superior laryngeal nerve is main factor responsible for afferent arch of laryngospasm.

Hence 4% or 10% xylocaine spray of supraglottis can prevent laryngeal spasm.

Extubation of bronchoscope when child is very deep and then keeping child in head down and lateral position, so that secretions do not enter larynx, will certainly prevent laryngospasm.

If laryngospasm does occur don't panic, give oxygen under pressure with face mask and press mastoid tip, it does open up. If not, give suxamethonium 0.5 mg/kg and intubate with appropriate sized endotracheal tube.

2) **Laryngeal Oedema:** This is a complication due to poor surgical technique in the form of rough handling and overall manipulation of bronchoscope at glottic level. I/V Steroids do help but in some cases one has to resort to tracheostomy to save the child. Ideally, proper instrumentation and thorough training is required to prevent this complication.

3) **Aspiration of Secretion or Vomitus:** This can be easily prevented by proper positioning at end of extubation. Proper suctioning of secretions from throat at time of extubation is very important.

Last word on bronchoscopy is, never get disheartened if you don't find foreign body in bronchus because it may be a case of laryngo tracheal bronchitis, pneumonia or some other congenital anomaly etc. In order to confirm your findings, you get bronchoscopy done from more experienced surgeon.

Since foreign body aspiration is a dramatic event with potentially lethal sequelae. Education is the best preventive measure for decreasing the incidence of this problem.

ACKNOWLEDGEMENT

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Radlcal Vs Conservative Approach For Orbital Lesions

Rafiq Ahmad, Hakim Arshad, Nursat Shaheen

Abstract

The vision of man has enabled him to make enormous progress and emerge as supreme species.The basic anatomical unit of vision, ocular apparatus is housed in a four sided pyramid -the orbit. The orbit represents an important cross-road of the central nervous system,the nose and paranasal sinuses, the face and structures related to support the eyes.

The orbit is often invaded by the lesions from ENT surgeon's and Neurosurgeon's domain. The ENT surgeon is involved in the surgery of the orbit quite often as an ENT surgeon , endoscopic surgeon and now also as skull base surgeon. In this presentation we have evaluated the role of radical versus conservative approaches for orbital lesions,particularly the role of endoscopic surgery in the orbit.

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Introduction:

Progressive proptosis is the most common symptom. Apical tumors and those within the muscle cone push the eyeball forwards (axial proptosis). Extraconal tumors displace the eyeball in the opposite direction. A hyperostosing sphenoidal meningioma produces prominence of the lateral wall. Pulsatile exophthalmos in neurofibromatosis suggests a defect in the sphenoid bone.

MRI is the imaging of choice. It is particularly valuable in assessing the orbital pathway because of the high degree of sensitivity of fat tissue, changes of hydration within the soft tissue, and lack of ionizing radiation. Gadolinium MRI adds to better delineation.

- A *CT* may help to visualize the bony involvement better. Plain x-rays have become obsolete.
- Carotid *angiography* helps in evaluation of CCF and orbital AV fistula.
- Duplex *ultrasound* is useful to assess the haemodynamic flow in the ophthalmic and retinal arteries.

Biopsy

- A,FNAC
- It is done when mass is palpable or can be approached safely. It is better to do Usg\CT guided FNAC. Vascular lesions should not be biopsied, angiography is preferable.
- B,Open Biopsy
- If FNA is inconclusive, it is preferable to do open biopsy before radical surgery. It can be done through one of the orbitotomy approaches.

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Present Series:

Total No. of cases: 23

Primary Orbital Lesions	Histological diagnosis	Para-orbital lesions	
Traumatic haematoma	3 patients	Sq.Cell Ca of Nose	2 patients
NHL	2 patients and PNS		
Squamous Cell Carcinoma	2 patients	Frontoethmoidal Mucocele	4 patients
Menigngioma	2patients		
Malignant Melanoma	1patient	Rhabdomyosarcoma Nose	1patient
Pleomorphic adenoma	1patient		
Orbital osteoma	1patient	Olfactory Neuroblastoma	2patients
Lipoma	1patient		
		Inverted Papilloma	1patient

Case reports:

1.A 45 year old female presented with proptosis . CT Scan showed left side extraconal mass occupying superiolateral quadrant of orbit, the tumor was excised through lid crease incision laterally. HPE revealed pleomorphic adenoma.

2. A 14 year old boy presented with extreme degree proptosis , eye coming out, about 2 cms, out of globe with complete loss of vision.CT revealed huge bony tumor invoving the whole orbit with intracranial extension.The tumor was removed through anterior craniofacial approach using bicoronal incision ,anterior craniectomy and exenteration of the orbit was done.

3. A 55 year old male presented with proptosis and loss of vision of right eye with black pigmentation.FNAC revealed malignant melanoma , complete exenteration of the orbit was done.

4.Endoscopic decompression was done in a patient of orbital hematoma and also one benign tumor of the medial orbit was removed endoscopically.

5.A 25 year female presented with proptosis, pushing the eye-ball downwards and laterally.CT scan revealed calcified lesion of orbit extending to anterior cranial base.Craniofacial resection was done.

Surgical Approaches used :

1.Lateral orbitotomy	3 patients
2. Weber Fergusion Incision with lateral rhinotomy	3 patients
3.Medial orbitotomy with lateral Rhinotomy	5 patients
4.Endoscopic Decompression of orbital heamatoma	3 patients
5.Endoscopic surgery for Frontoethmoid mucocele	4 patients
6. Lid-crease incision	1 patient
7. Bicoronal incision with craniofacial surg.	2 patients
Radiotherapy	2 patients of NHL

Discussion :

The orbit has bony walls common with all four paranasal sinuses: 1) the orbital floor is part of the maxillary Sinus roof :.2) the medial wall is bordered largely by the lamina papyracea ot the ethmoid; '3) the roof of the orbit is com-prised partly of the floor of the frontal sinus and the floor of the anterior cranial fossa: and (4) the medial orbital apex is bordered ,by the lateral wall of the sphenoid sinus. Posterolaterally the greater wing of the sphenoid bone contributes to the bony orbit, such that it is adjacent to the anterior aspect of the middle cranial fossa. The optic nerve is dehiscent in the lateral sphenoid sinus wall in about 4o% of patients. These common bony walls are traversed by several named and unnamed foramina and fissures through which the nerves and vessels pass to and from the orbit.

- The management of orbital tumors greatly depends on such factors as tumor type, tumor location, patient age, and vision. However, the following generalizations can be made. Orbital inflammatory syndrome (orbital pseudotumor) may be amenable to steroid treatment. If the orbital lesion is discrete, then surgical excision may be curative. Examples of discrete lesions include cavernous hemangioma, unruptured dermoid cysts, neurofibromas and schwannomas.
- If the orbital lesion infiltrates the tissues, complete excision may not be possible without harming the eye. Examples of infiltrative lesions include lymphoma, lymphangiomas, and orbital metastases.
- Depending on the type of tumor, further surgery, radiation, chemotherapy or a combination of the aforementioned treatments may be required.
- Vascular orbital tumors composed of large blood vessels are difficult to address surgically because of their tendency to bleed. Some vascular lesions of the orbit are amenable to embolization with the aid of an interventional radiologis
- Restoration of the proptosed eyeball to its normal position with preservation of vision and ocular motor function and cosmesis are the main goals of orbital surgery. Surgical spaces in the orbit are used to define the location of the lesion.
- The three surgical spaces are the subpersiosteal, peripheral surgical and central surgical spaces.
- **(a) subperiosteal space:** The potentially exists between the orbital wall and the periorbita. Frontal and ethmoidal sinus mucocoeles, epithelial tumors arising from sinuses, orbital abscesses, dermoid cysts and metastases begin in the subperiosteal space before encroaching onto the deep orbital structures.
- b) **The peripheral surgical space :** exists between the periorbita and the extraocular muscles. Lesions involving the peripheral surgical space are lymphangioma, hemangioma, dermoid cyst, lacrimal gland tumors, metastatic lesions or orbital varices.

c) **The central surgical space** is seen posterior to the eye-ball, within the muscle cone. In the central surgical space cavernous hemangioma, hemangio-pericytoma, neurofibroma and pseudotumor are the lesions commonly seen.

Lateral orbitotomy: In 1889, Krönlein first described the lateral orbitotomy approach, it provides the best access to reach the posterior lesions both within and outside the muscle cone. Ideally, the lesions lateral to

the optic nerve and the apex are dealt with by this approach. The amount of bony excision can be customized to include more of the superolateral orbital rim, and even the zygomatic arch when necessary, depending on the size and location of various lesions. Most retrobulbar and parabulbar lesions can be handled by an anterior or lateral orbitotomy alone or in combination

Fronto-orbital temporal (Panoramic) approach:

This procedure allows for an en bloc excision of the roof and lateral wall of the orbit and a wide view of both the orbit and adjacent intracranial structure. This approach consists of a coronal incision and removal of the frontal flap in the usual manner followed by dissection of the temporalis fossa and elevation of periorbita from the adjacent bone. An incision is then made along the superomedial wall of the orbit after distracting the frontal lobe from above. The bony incision is extended along the roof of the orbit to the lateral margin near the apex, whence the lateral wall and frontozygomatic process are incised. With removal of the bone a wide view of the roof and lateral orbital structures is obtained. This approach is particularly useful for excision of tumors at the apex of the orbit or for combined intracranial orbital lesions such as tumor of the optic nerve or sphenoid wing.

Extraperiosteal approach:

The anterior extraperiosteal approach is most useful for lesions occurring in the peripheral surgical space adjacent to periosteum or arising from and involving bone. In particular, lesions such as dermoid cysts are readily accessible by this approach. The skin incision is usually made just at the orbital rim and carried down to the periosteum, which can then be incised and elevated. The extraperiosteal space can then be safety and extensively explored.

Inferior Approach: An alternative route of access inferiorly can be by means of subsciliary incision through skin and orbicularis muscle with dissection along the plane of the orbital septum and incision of the periosteum at the orbital margin. The entire floor of the orbit can be easily explored.

Superior approach: The superior approach is necessarily the domain of neurosurgeon. Dandy in 1921 laid the foundation for Neurosurgeon's role in orbital tumors with transcranial approach. The superior approach indicated in compound trauma of the orbit and intracranial cavity, decompression of the optic canal, or for removal of apical or combined apical intracranial lesions. There are three types of procedures used for this approach: Panoramic orbitotomy (Fronto-orbital temporal approach), Frontal approach, Supraorbital approach.

Combined approach: All of the approaches defined above can be used in combinations or with variations to obtain access to any of the surgical spaces of the orbit. Widening bony incisions and even removing part or all the sinus structures to expand the surgical space may rarely be necessary.

Endoscopic Appraoch: Endoscopic approach is the new approach used by the ENT surgeons who are well versed with the endoscopic sinus surgery.The lesions like orbital haematoma , fronto-ethmoid mucoceles and benign orbital lesions particularly of medial orbit can easily be removed endoscopically.In this series we have drained 3 post traumatic orbital haematomas endoscopically but the vision could not be restored as patients were referred late to us, for saving vision the haematoma should be drained within 12 hours.We also drained four fronto-ethmoid mucoceles presenting with proptosis and removed one benign orbital tumor through endoscopic approach.

We have used craniofacial approach in two cases using bicoronal incision . It is an excellent approach and cosmetically much better than weber-furguson and lateral rhinotomy approaches , the scar is invisible as it remains hidden in the hair line. The lid crease approach for lateral orbital benign lesions gives least scar.

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The Effect Of Trabeculectomy On Corneal Astigmatism

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Abstract

Recently surgery for glaucoma is being performed at early stages of the disease when the vision is still fairly good . Many patients report subjective changes in vision following trabeculectomy . Surgically induced astigmatism is becoming an important issue because it delays visual rehabilitation and exerts a negative effect on the final visual outcome . The study was conducted on 100 patients , 86 males and 14 females , whose age ranged from 35- 75 years . Two types of astigmatic changes were found following trabeculectomy . 87 % of patients showed vertical steepening and ' with the rule ' astigmatism , while 13 % showed vertical flattening and 'against the rule' astigmatism . The surgically induced astigmatism was more in the early post operative period and decreased with time . The astigmatism lasted till the end of the study which was a period of three months . The impact of the procedure on the visual prognosis of the glaucoma patient must therefore be carefully evaluated .

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INTRODUCTION

Trabeculectomy is a filtering procedure which lowers the intraocular pressure by creating a new channel for aqueous outflow between the anterior chamber and sub-tenon space .

Corneal astigmatism following cataract extraction is now well recognized. There is an increase in the vertical corneal radius of curvature. In contrast in trabeculectomy there occurs a reduction in the corneal radius in the vertical meridian . The reason of this difference may be the result of partial thickness scleral flap created during trabeculectomy . The surgically produced gap is overlaid by a scleral flap , which spreads support from the sutures inserted into it over the whole of the wound gape . the more posterior placement of the incision may also explain the difference in behaviour in comparison with cataract extraction[1].

MATERIAL AND METHODS

The study was conducted in the Department of Ophthalmology , Government Medical College , Srinagar . One hundred patients who reported to the Ophthalmology out patient department with the diagnosis of primary open angle glaucoma uncontrolled with maximal medical therapy and needing filtration surgery were included in this study . The exclusion criteria included :- previous intraocular surgery , significant corneal opacification , patients needing combined surgery , congenital / juvenile glaucoma and patients having best corrected visual acuity less than 6/60 .

Trabeculectomy was performed under local anaesthesia . The visual acuity , subjective refraction and manual keratometry readings were recorded pre-operatively and post-operatively at two weeks , one and three months . The Bausch and Lomb Keratometer was used .

All post operative keratometry readings were compared with the pre-operative values by the paired t-test. Results were given as mean (SD).

OBSERVATIONS AND RESULTS

The distribution of age and sex of the patients is given in tables 1 and 2 respectively .

Table 1: Age distribution of patients

Cases	Range	Mean ± S.D
Age in years	35-75	58.47 ± 7.40

In our study age in years ranged from 35 -75 yrs.

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KEYWORDS *: Trabeculectomy, Surgically induced astigmatism , Vertical steepening, Vertical flattening .*

The mean age was 58.47 ± 7.40 yrs.

Table 2: Sex distribution of cases.

Cases	Number	Percentage
Male	86	86.00
Female	14	14.00

In our study 86% of patients were males and 14% were females.

Table 3: Vertical Keratometry changes in vertical steepening group [Group I]

Stage	Mean ± S.D [Diopters]	t – Value	p – Value
Pre-operative	43.89 ± 1.49		
Post-operative 2 weeks	45.14 ± 1.50	62.17	.000
1 month	44.84 ± 1.49	43.38	.000
3 month	44.56 ± 1.49	35.04	.000

Two types of astigmatic changes were found following trabeculectomy . 87 out of 100 patients showed vertical steepening and 'with the rule' astigmatism (Group I) , while 13 out of 100 patients showed vertical flattening and 'against the rule' astigmatism (Group II) .

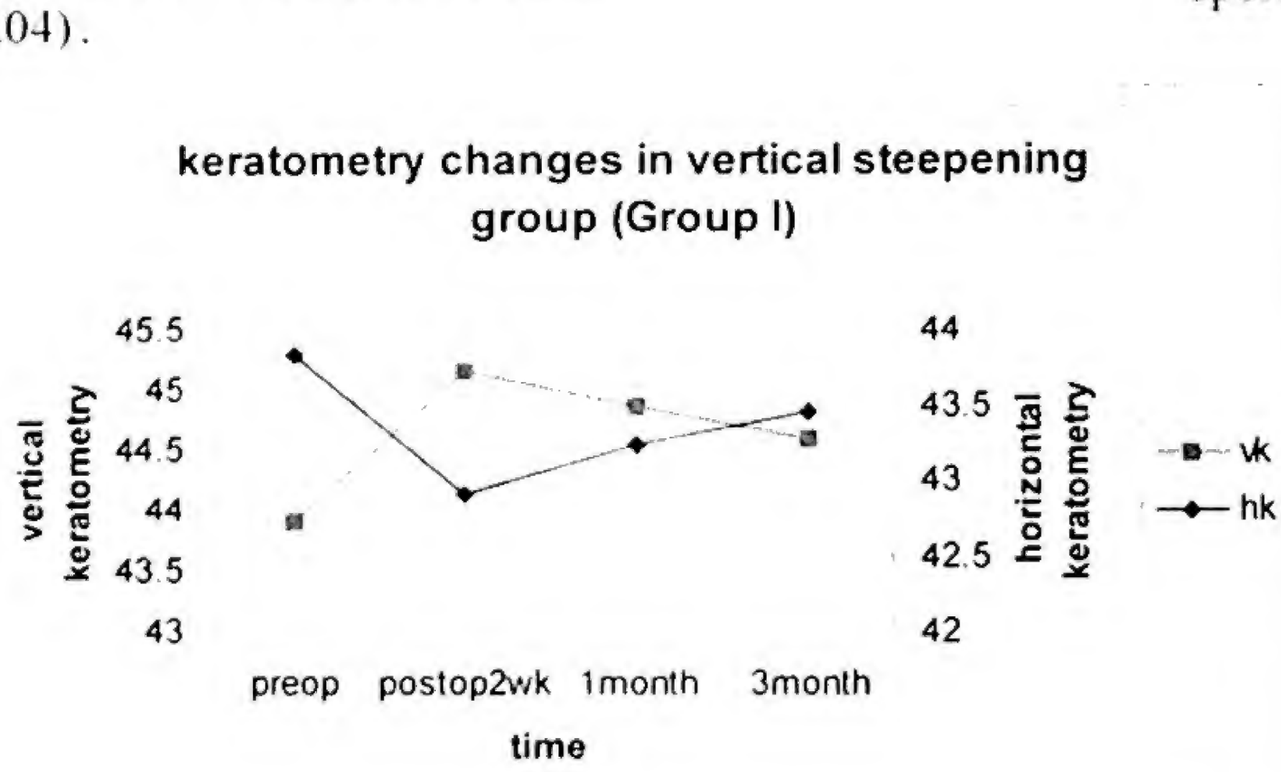
Table 4: Horizontal keratometry changes in vertical steepening group. [Group I].

Stage	Mean ± S.D [Diopters]	t – Value	p – Value
Pre-operative	43.82 ± 1.58		
Post-operative 2 weeks	42.89 ± 1.58	51.778	.000
1 month	43.21 ± 1.59	31.089	.000
3 month	43.44 ± 1.57	22.786	.000

There is a statistically significant difference (p-value of 0.000) between the pre-operative and the post-operative vertical keratometry reading at 2 weeks, 1 month and 3 months. The difference is more during the early postoperative period (t-value 62.17) and becomes less by the end of 3 months (t-value 35.04) .

Table 5 : Vertical keratometry changes in vertical flattening group [Group II]

Stage	Mean ± S.D [Diopters]	t – Value	p – Value
Pre-operative	43.81 ± 1.34		
Post-operative 2 weeks	43.00 ± 1.43	14.00	.000
1 month	43.25 ± 1.43	9.667	.000
3 month	43.46 ± 1.40	7.675	.000



Manual keratometry data in the vertical steepening group indicated an increase in the vertical keratometry values and a decrease in the horizontal keratometry values. The decrease in horizontal keratometry reading at 2 weeks postoperatively was more (t-value 51.778) as compared to the decrease in the horizontal keratometry value seen at 3 months postoperatively (t-value 22.786) with a p-value of 0.000.

There is a statistically significant difference between the pre-operative and post-operative vertical keratometry reading at 2 weeks (t-value 14), 1 month (t-value 9.667) and 3 months (t-value 7.675). with a p-value of 0.000.

The vertical flattening group showed a decrease in the vertical keratometry readings and a statistically significant increase in the horizontal keratometry readings. The increase in the horizontal keratometry readings was more at 2 weeks postoperatively (t-value 38.00) as compared to the horizontal keratometry reading at 1 month (t-value 25.00) and 3 months (t-value 11.08) postoperatively with a p-value of 0.000.

The mean vertical steepening was 1.1 Dioptre and the mean vertical flattening was 0.7 Dioptre at 3 months.

Three months post-operatively 63 eyes maintained their pre-operative visual activity, 28 eyes lost 1 line, while 9 eyes lost 2 lines of Snellen's visual activity.

DISCUSSION

Trabeculectomy affects the corneal curvature. In the majority of the patients (87%) the vertical corneal radius of curvature was reduced with a trend towards 'with the rule' astigmatism. The horizontal radius of curvature was increased. Thus there was steepening in the vertical meridian.

In 13% of patients the vertical radius of curvature of cornea was increased and horizontal radius of curvature was decreased, causing 'against the rule' astigmatism. There was flattening in the vertical meridian.

These changes were marked in the early post-operative period and decreased by the third post-operative month.

Hugkulstone[1] (1991) found similar changes in the vertical corneal radius of curvature following trabeculectomy in 10 patients.

Rosen et al[2] (1992) found that five of eight eyes developed 1.50 to 2.50 diopters of steepening in the 90-degree meridian following trabeculectomy. This finding is in accordance with our study

Cunliffe IA et al[3] (1992) discovered that the change in vertical corneal curvature after trabeculectomy is consistent with the with-the-rule change in corneal astigmatism. This supports our finding.

Claridge et al[4] (1995) suggested that there appear to be two broad patterns of topographic variation following trabeculectomy, the most common being a postoperative steepening of the corneal curvature though a smaller number of patients developed a superior corneal flattening.

Liu et al[5] (1996) found that trabeculectomy may cause certain with-the-rule corneal astigmatism which in most of the cases may decrease as time passes by.

Dietze et al[6] (1997) concluded that by 12 weeks after trabeculectomy, visual acuity returned to preoperative levels in all patients and the corneal topographic changes returned to within 1 diopter of preoperative values in 12 of 13 patients. In the study we conducted, the visual acuity of majority of patients (63%) returned to preoperative levels and the mean surgically induced astigmatism was 1.1D in the superior steepening group and 0.7D in the superior flattening group.

Various explanations have been given regarding the effect of trabeculectomy on corneal curvatures.

In trabeculectomy the surgically produced gap is overlaid by a scleral flap. This is capable of spreading any support from the sutures inserted into it over the whole of the wound gape.

In addition the more posterior placement of the incision in trabeculectomy may also explain the observed behaviour as the size and location of the incision have a profound impact on the postoperative visual results[1].

Another explanation is that in trabeculectomy, when a piece of tissue is removed from under the scleral flap and the flap then sutured back, the flap approximates the corneal edge of the trabeculectomy opening to the scleral edge and also allows the unsupported corneal edge of the opening to sink slightly. Both of these mechanisms would have the effect of shortening the vertical corneal radius of curvature. A few months onwards the tension in the sclera sutures may start to weaken and allow the free corneal edge of the sclerostomy opening to resume its preoperative position[1].

The cause of induced astigmatism may be related to the use of cautery during surgery, producing a contraction of the sclera in the meridian of surgery and leading to the 'with the rule' astigmatism[7].

Hong YJ et al[7] (1998) suggested that mitomycin –C (MMC) induces less with the rule astigmatism in the early postoperative period and continuous against the rule shift after three months following a trabeculectomy. The inhibition of fibroblast proliferation by MMC may be the cause of less with the rule shift.

Vernon[8] (1999) discovered that small flap trabeculectomy produces smaller changes in corneal curvature that resolve sooner than previous reports of larger flap technique.

Thus, following trabeculectomy, the changes in corneal curvature affect the central cornea, but they are not reflected in any marked change in the visual acuity by the end of the study. Long term studies are required to investigate whether these changes continue to evolve, as has been shown to occur following cataract extraction.

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Original Article

Feasibility of Diagnosis and typing of porphyrias in developing countries like India -its biochemical basis.

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Abstract

The 'Porphyrin –profile' based on definitive picture of accumulation and hyperexcretion of porphyrins(PPNs) and their precursors is effectively used for diagnosis and typing porphyrias. Here spectrophotometric measurement of porphyrin(PPN) type after extraction and differentiation by solvent partition has been effectively used as a substitute to exact isomer identification by HPLC which is not usually available in most hospitals of developing countries .Over a period of two years. out of 155 suspected patients screened for porphyria , 8 porphyria patients have been successfully diagnosed and typed . Three exemplary chosen cases of porphyria so diagnosed have been discussed to elucidate the 'ruling out regime' followed for diagnosis. Our report can serve as a prototype for porphyria diagnosis/typing in similar centers of developing countries .

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Introduction :-

Porphyrias form a group of seven different types of rare metabolic disorders of heme biosynthesis, inheritable and acquired .They are characterized by aberrations in the activities of specific enzymes of heme biosynthetic pathway. Basis of porphyria typing is the defective enzyme of heme biosynthetic pathway , its site of expression and the resultant pattern of production and excretion of PPNs and their precursors. They may be classified pathologically as "hepatic" and "erythropoietic" types, depending on the principal site of expression of enzymatic defect . Clinically the principal symptomatology ranges from cutaneous photosensitivity, to photosensitivity with neurovisceral symptomatology to purely neurovisceral symptoms only- depending on the type of porphyria. Porphyrias with skin manifestations are sometimes called "cutaneous porphyrias " and "acute porphyrias" are those characterized by sudden attacks of pain and other neurological manifestations . Aminolevulinic acid dehydrase (ALAD) porphyria and acute intermittent porphyria (AIP) cause predominately neurovisceral symptoms(acute abdominal pain,neuropathy, autonomic instability, psychosis, etc.), whereas congenital erythropoietic porphyria (CEP), porphyria cutanea tarda (PCT), and erythropoietic protoporphyria (EPP) cause mostly cutaneous symptoms. Two porphyrias overlap these categories causing both neurovisceral and cutaneous symptoms, namely hereditary coproporphyria (HCP) and variegate porphyria (VP) [1-4]

Porphyrias being rare are sometimes missed or misdiagnosed because its various signs and symptoms mimic other diseases . Laboratory tests termed as 'Porphyrin –profile' are effectively used for diagnosis and typing of porphyrias .Enzyme assays and mutation screening are mainly used for family studies [2]. Porphyria typing is essential as the protocol for management of porphyria patients differs for various types. Early diagnosis and information about precipitating factors can diminish mortality and prevent subsequent attacks especially among patients with acute porphyrias[2].

Patients and Methods :

Over a period of two years a total of 155 patients presenting with symptoms of cutaneous photosensitivity, photosenitivety with neurovisceral symptoms and/ or purely neurovisceral symptoms were screened for porphyria as the possible cause of symptoms and then positive cases were further typed . Clinical examination was carried out.

Key Words :*Porphyrias, Porphyrins , Porphyrin Precursors, Porphyria-Profile.*

Table 1.

First-line testing for patients in whom porphyria is suspected as a cause of symptoms	*Most sensitive & specific test for screening*
Symptoms	Urinary PBG and delta-ALA (total Urinary PPN determination is also recommended)
Neurovisceral	Total Plasma porphyrins
Skin photosensitivity	

Investigations included routine relevant hematological and biochemical tests and the 'Porphyrin- profile' based on the pattern of production and excretion of PPNs and their precursors which varies in in different types of porphyrias . The 'porphyrin –profile ' comprises of qualitative and quantitative analysis of PPNs in urine (24h), stool, plasma and erythrocytes and PPN precursors ,delta-aminolevaleunic acid (ALA)and porphobilinogen(PBG)in urine. Porphyrins are tetrapyrroles and in their oxidized form are reddish in color and fluorescent, they appear intensely red when exposed to long-wave ultraviolet light (UV-A) this makes them visible under a Wood's lamp . They can be measured accurately spectrophotometrically. Within cells all porphyrin intermediates of heme excepting protoporphyrin are in reduced form thus colorless and nonfluorescent ,but PPN's that leave the cells and appear in blood , urine feces are mostly oxidized . As HPLC needed for exact porphyrin isomer identification [4-6] is unavailable in most hospitals in developing countries in our laboratory alternatively , PPN type and not the isomer, was spectrophotometrically measured after extraction and differentiation by solvent partition [4-6,10] A 'Ruling out regime' was followed wherein by taking cognizance of the porphyrin-profile and clinical picture exact porphyria typing was possible. As is exemplified by following chosen cases of porphyria diagnosed.

Results and case reports :

Case Report A :

A 30 year old female having three offspring was being managed for uncontrolled hypertension .While managing her for the same,clinical examination revealed certain striking features of cutaneous-photosensitivity, hyperpigmentation, hypertrichosis,pinched nose, sclerodermoid changes,erythrodontia,oncholysis of terminal phalanges and pallor along with history of passing red colored urine since childhood. Abdominal examination revealed splenomegaly.(Figure1). Routine investigations revealed hemolytic anemia with Negative Coomb's test Porphyrin- profile results showed increased urine , stool, erythrocyte and plasma PPNs . Normal ALA and PBG levels . Quantitative studies revealed urinary PPN leves (>50 times above normal) with uroporphyrin levels more than coproporphyrins (ratio >5:1) and elevated fecal PPN levels with coproporphyrin levels more than uroporphyrins(ratio >7:1). Erythrocytes showed greatly increased coproporphyrin levels with small amounts of uroporphyrins (ratio >9:1), protoporphyrins levels were near normal.

Case report B :

A 40 year old male presented with cutaneous lesions on light exposed areas of the dorsa of hands and face.History revealed that sun exposure led to formation of vesicles and bullae. healing took place with crusting and scar formation. since past four years Cutaneous examination revealed hyperpigmentation with scarring on face and dorsa of hands. Above mentioned investigations were carried out. Significant revelations were raised S. Iron levels (187 ug/dl). raised serum transaminases AST(89U/L). ALT(84 U/L) and T. Bilirubin (1.6 mg/dl). As per porphyria profile PBG and ALA levels were normal. PPN levels were raised in urine,stool and plasma but not in erythrocytes. Quantitative studies revealed that urinary PPNs were greatly elevated uroporphyrin levels being more than coproporphyrins (ratio >5:1).Fecal PPN levels too were greatly elevated, here coproporphyrin levels were more than uroporphyrins (ratio 8 : 1).(Figure 2)

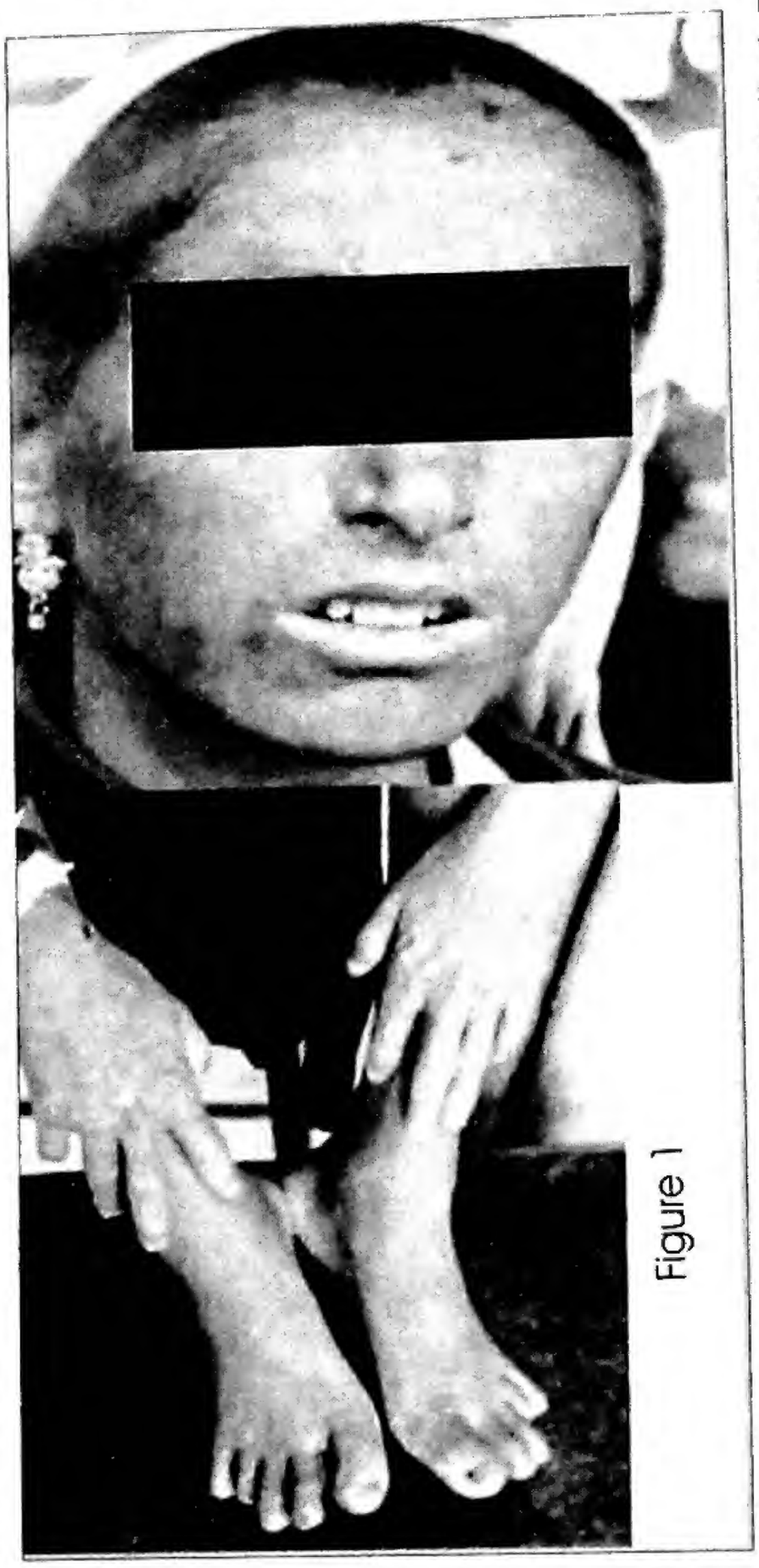

Figure 1

Case Report C ;

A 15 year old boy born of consanguineous marriage with normal siblings having history of cutaneous photosensitivity since age of four years presented with pruritic ,bullous lesions on face, ears and hands . On cutaneous examination hyper and hypo pigmented lesions with scarring and milia formation were observed on face, ears and hands. Healing was with scars and milia formation. Short stature and pinched nose was observed. Abdominal examination revealed

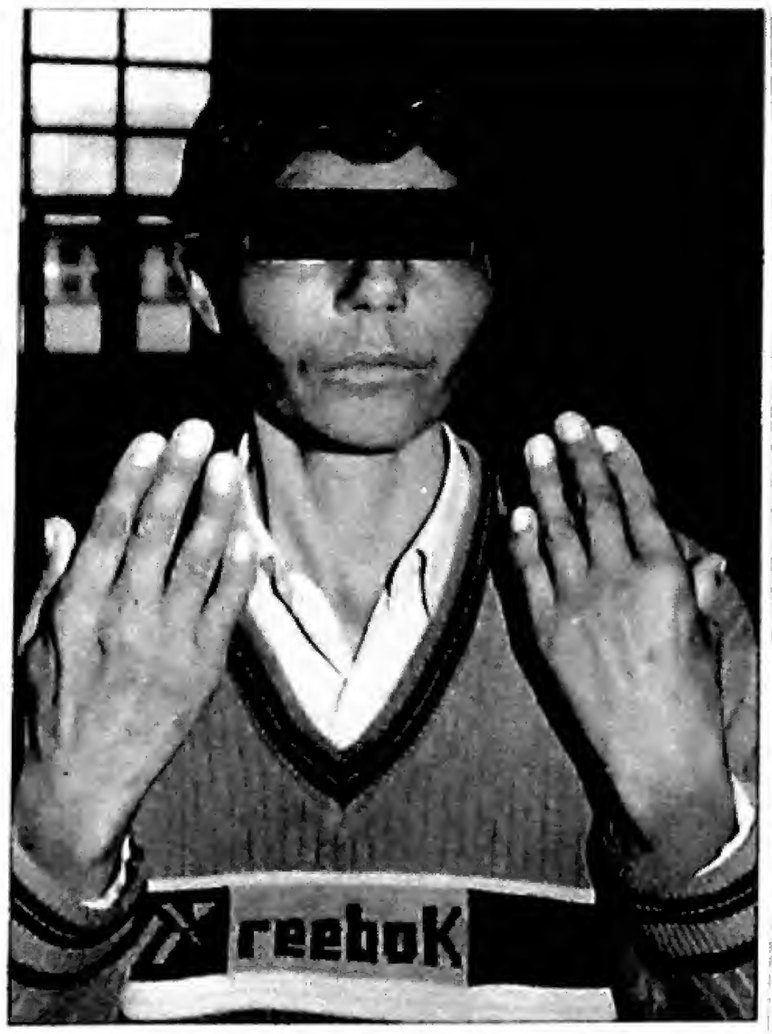

Figure 2

splenomegaly. All above specified relevant investigations were carried out. Routine investigations signifantly revealed hemolytic anemia with negative Coomb's test. As per porphyria profile, ALA and PBG levels were normal. PPN levels were raised in stool and erythrocytes only. Quantitative studies revealed greatly elevated fecal PPN levels , here coproporphyrin levels were more than uroporphyrins, with significant amounts of protoporphyrins as well. Erythrocytes showed greatly increased levels of protoporphyrins (> 80 %),which were free as shown by ethanol extraction .

Dicussion :

In past, it was customary to obtain many or all available tests when porphyria was suspected and then compare any abnormal results with tables showing patterns of abnormalities to be expected in the seven types of porphyrias . Latest , less costly approach is to rely on a few well chosen "first line"/ screening tests that are both sensitive and specific thus avoiding misdiagnosis.If these are normal, the possibility of porphyria as a cause of symptoms is effectively ruled out. If positive, further testing by "second-line tests" are needed for porphyria typing. No single test is effective for screening of all porphyrias. However, one of two tests can be relied upon in almost all situations, depending on the symptoms as depicted in table I [1-4]

Thus by a 'ruling out regime' porphyria can be ruled in or out in many patients with nonspecific symptoms with only one or a few tests. Porphyria is ruled out much more commonly than it is ruled in. This regime was followed and by taking cognizance of laboratory results and clinical picture porphyria typing was done as is exemplified by following three cases of porphyria.

Regarding case A, striking features especially hypertrichosis, cutaneous photosensitivity, resorption of distal phalanges with a history of passing red colored urine – pointed towards porphyria . Erythrodontia observed was pathognomonic of CEP (Figure 1). A picture of increased urine, stool, plasma and erythrocyte PPNs on screening was highly suggestive of CEP[1,4,12] or a variant of PCT. Hepato Erythropoietic Porphyria (HEP)[13] A feature of erythropoietic porphyrias -urinary free PPNs fluorescing intensely under UV light without extraction was observed.[1,9]. Increase in plasma PPNs is a specific marker for cutaneous porphyrias.[2] Normal ALA and PBG levels rule out acute porphyrias .Other types are rendered unlikely on basis of this pattern of increase in PPN levels(qualitative studies) and clinical picture . Laboratory results revealed hemolytic anemia with negative coomb's test and splenomegaly, favoring CEP[11,14,15].Quantitative PPN studies revealed Urinary Uroporpyrin levels more than coproporphyrins ,elevated fecal PPN levels with coproporphyrin levels more than uroporphyrins favoring CEP. Erythrocytes showed greatly increased levels of coproporphyrins with small amounts of uroporphyrins, protoporphyrins levels were near normal again favouring CEP,[10,11, 14-17] as in HEP increased erythrocyte Zn- protoporphyrins are an important feature.[11,13] In CEP the primary abnormality is decreased URO cosynthase activity resulting in accumulation of type I PPNs [1,4,12]

As per case B , increased urine, stool and plasma PPNs with normal PBG and ALA point towards a non-acute cutaneous type of porphyria as the cause of observed cutaneous lesions [14]. (Figure 2) Normal level of erythrocyte PPNs rule out erythropoietic porphyria. Thus by the ruling out regime acute porphyrias and erythropoietic porphyrias are ruled out by first line /screening tests only. The choice in absence of neurovisceral symptoms narrows down to porphyria cutanea tarda [18-24] Routine laboratory tests revealed raised plasma iron levels a hallmark of PCT,observed raised transaminases too are a feature of PCT [25]. This is established further by quantitative analysis as Urinary Uroporphyrin levels more than Coproporphyrin again favour PCT over VP or HCP [19,21]

As per case C , the clinical picture of cutaneous photosensitivity with hemolytic anemia demanded porphyria screening. Increased stool, and erythrocyte PPN levels only with normal levels of ALA and PBG point towards non- acute type of porphyria. Quantitative studies revealed normal urinary PPN levels with greatly increased levels of erythrocyte protoporphyrins alongwith increased fecal coproporphyrin and protoporphyrin levels favouring EPP [1,4,11,26]. Observed normal plasma levels of protoporphyrins can be accounted for as they are very light sensitive and get destroyed very fast in the plasma before they can be assayed [27,28] The enzymatic defect in EPP being partial deficiency of ferrochelatase activity resulting in protoporphyrin accumulation primarily in erythroid cells[1,4,26]

Conclusion :

Thus, by using abovementioned techniques and following the 'ruling out regime' porphyrias can be possibly diagnosed and typed in most of the hospitals of developing countries like India. Thereby improving patient care in these centers with nearly existing infrastructure and not much further investment.

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Case Report

A benign mature cystic sacrococcygeal teratoma in a patient aged 3½ years

Masood Iqbal, Akram Hussain, Intikhab Alam, Adil Rashid, M.N. Ahmad

Abstract

We describe a case of sacrococcygeal teratoma in 3 ½ year old female child, who presented as a swelling in sacral region since she was 2 months old. She was admitted for evaluation and FNAC of the swelling revealed features of teratoma, however needed confirmation on excision. USG and CT scan revealed a cystic lesion in front of sacrum pushing the rectum and gut anteriorly and extending below and behind the coccyx and sacrum. Excision of the cystic lesion was done and specimen sent for HPE, which revealed the features of benign mature cystic teratoma. The patient was followed for one year on OPD basis and showed no evidence of recurrence of growth, with full control of bowel and bladder.

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Introduction: - Sacrococcygeal teratoma accounts for 32% to 66% of non-gonadal germ cell tumours. It is the most common tumour of new born occurring in about 1 in 35,000 births.[1]

60% of sacrococcygeal tumours are diagnosed at birth and only 6% come to clinical attention after the age of two years.[2]

The incidence of tumour malignancy is related to the age of the patient at the time of diagnosis. When the tumour is found before the age of 1 month, the risk of malignancy is only 5%, between 1 to 12 months of age the malignancy rate is 60% and in children older than1 year of age over 75% of germ cells of sacral region are malignant. Malignant tumours are more common in boys.[2]

These tumours more commonly present clinically as a large midline exophytic mass located posterior to the sacrum. The anus is usually displaced anteriorly.

Differential diagnosis includes lipoma, meningocele, dermoid cyst, and a host of other tumours or malformations.[1]

Associated congenital anomalies are seen in about 20% of the patients, usually of musculoskeletal in origin fallowed by abnormalities of kidneys, CNS, heart and alimentary tract.[2,4,5] In addition, the Currarino triad can be associated.[3] This syndrome is inherited as autosomal dominant manner, consisting of a presacral tumour, anorectal stenosis and sacral bony abnormalities. This underscores the importance of DRE in these children. Aside from the obvious tumours other associated signs and symptoms are high output heart failure due to vascular shunting through the tumour, birth dystocia occasionally seen owing to tumour bulk. 25% of sacrococcygeal teratomas are discovered on antenatal sonogram.

Radiological evaluation includes A-P and lateral radiographs of the pelvis and spine. Calcifications are the frequent findings in teratoma. The sacral spine may reveal a defect suggesting invasion of the spinal canal by the tumour or that the lesion is not the teratoma but rather some anomaly of spinal cord. USG, CT scan, MRI can be useful in determining the pelvic abdominal extent of the tumour as well as its anatomic relations to the adjacent structures.[1]

A Chevron type incision is made and the tumour is removed with the coccyx, care should be taken to avoid injury to the anus & rectum. Failure to remove the coccyx results in local recurrence rate of about 37%[1].

About half of sacrococcygeal teratomas have a significant pelvic or abdominal component (AAP classes II & III) and 15% of such lesions are entirely presacral with no external component (AAP class IV).[2]

Key Words: - *Sacrococcygeal Teratoma, Germ cell tumour, Benign, New born.*

As expected the outcome of children with sacrococcygeal teratomas is related to the presence of malignancy within the lesion and stage of disease at the time of diagnosis.

Stage I Complete tumour resection with negative margins

Stage II Microscopic residual disease negative lymph nodes

Stage III Gross residual disease or biopsy only nodes positive or negative

Stage IV Distal metastasis

Surgical resection is curative in most benign tumours. The long term survival rate of neonates after surgery is 92 – 95 %."

CASE: -

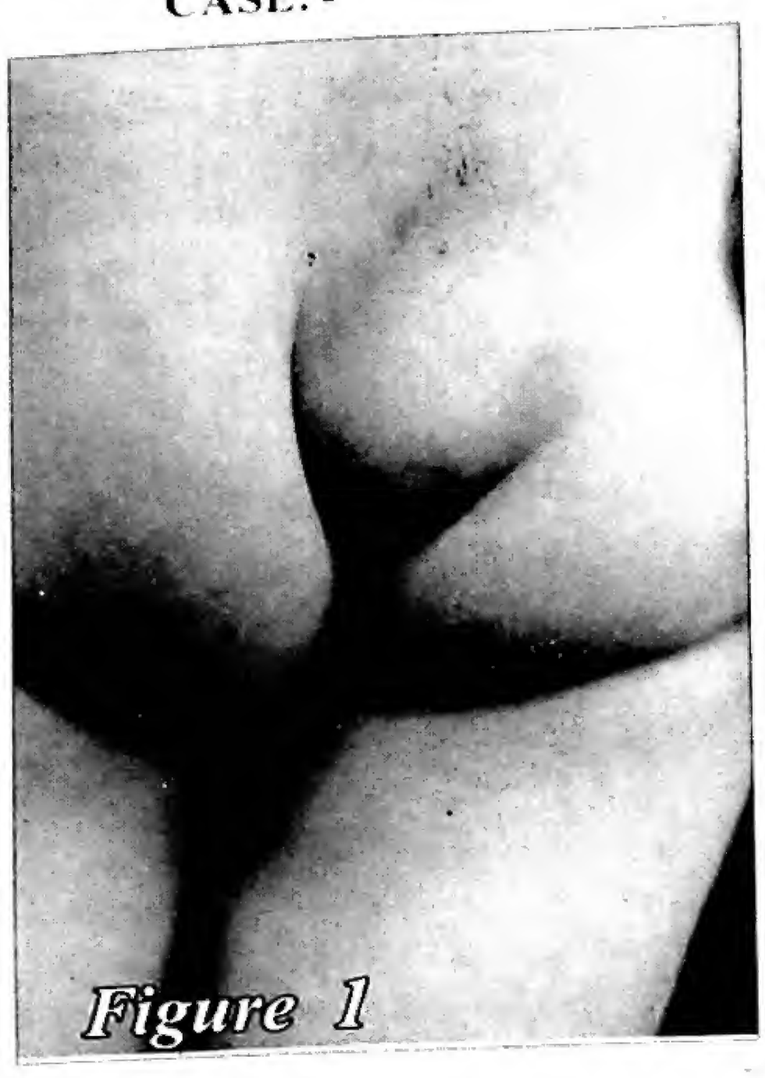
Figure 1

A 3 ½ year old female child belonging to Gujjar community reported in the outpatient department with chief complaints of swelling in anal region **(Fig 1)**. The patient was admitted for evaluation.

Her parents gave history that she was a full term baby delivered normally at home with no history to suggest any birth complications.

The mother of the patient first noticed the swelling around the anal region on back side when the patient was two months old. Initially the swelling was the size of a grape which used to become more prominent during defecation. The swelling steadily increased in size as the patient grew up. Finally the parents thought of seeking medical advice when the patient was 2 ½ years old. The doctor who attended the patient advised the parents to take the patient to SMHS hospital for surgical management. Patient was brought to this hospital when she was 3 ½ years old.

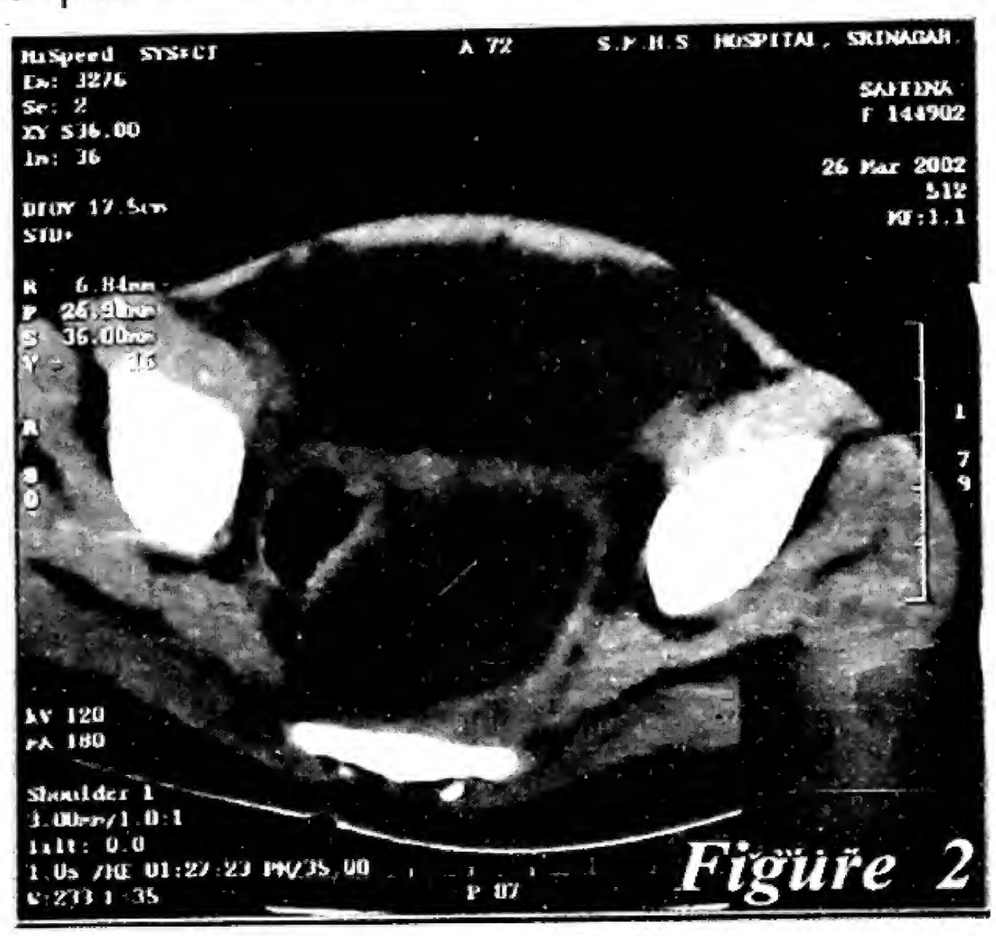

Figure 2

On examination the general condition of patient was fair with nothing abnormal detected on chest, CVS, CNS, and *per abdominal* examination. The growth and development was also within normal limits. The patient had a visible swelling **(Fig 1)** in the sacrococcygeal region of the size of a tennis ball with normal overlying skin. The swelling was globular, soft, smooth, and slightly movable and cough impulse was negative. It was non reducible & transillumination test was negative.

Figure 3

The per-rectal examination revealed a bulge posteriorly. She had a haemoglobin of 11.5g%, TLC: - 7500/cu mm, DLC: - P. L. Plasma sugar, KFT, was within normal limits; X- ray chest, abdomen and pelvis were non-specific. Abdominal USG revealed a cystic mass posterior to the urinary bladder. CT scanning showed a cystic mass anterior to the sacrum pushing the gut loops and rectum anteriorly **(Fig 2)**. The same cystic mass extending below and behind the coccyx and sacrum. Posterior arch of sacrum and coccyx were bifid. The swelling starts from S2 and has dimensions of about 6x3x2 cm. FNAC of the swelling reported as smears showing features consistent with cystic teratoma, however excision biopsy was recommended.

The patient was prepared for elective surgery, and services of paediatric surgeon sought for elective procedure.

UAAP a Cheveron incision was made and cystic lesion in the sacrococcygeal area separated from the surrounding adhesions. Tip of the coccyx was also divided to facilitate the removal of the swelling, which was removed enmass. **(Fig 3)**.

Haemostasis was achieved, two Redivac drains were kept & wound closed back. Specimen was sent for HPE to the Deptt. of Pathology, GMC Srinagar.

The postoperative period was uneventful and the patient had complete control over bowel and bladder function and was discharged on the 7th postoperative day.

Figure 3

The HPE report of the specimen revealed features of benign mature cystic teratoma.

The patient was followed up for one year on OPD basis and showed no evidence of recurrence. The patient was healthy and had full control of bowel and bladder.

DISCUSSION: - A benign mature cystic sacrococcygeal teratoma is rarely found after an age of 1 year. The higher frequency of malignancy with age parallels with the higher AAP anatomic class seen in older children.

Typically the patient present with severe constipation and are initially referred for evaluation of Hirschprungs disease. This underscores the importance of digital rectal examination in these children to evaluate the presacral region. In some of these children anal atresia or stenosis requiring surgical treatment is the presenting diagnosis.

In our case swelling in the sacrococcygeal region was the presenting complaint but digital examination revealed a bulge in the presacral region. There was no history of constipation, urinary retention, decreased appetite and failure to thrive.

Baseline investigations and specific like AP & lateral radiographs of investigations the pelvis and spine, USG, CT, or MRI can be useful in determining the pelvic and abdominal extent of the tumour as well as its anatomic relation to adjacent structures. MRI is particularly useful in evaluating infiltration into the spinal canal.

In most cases, surgery is the principal mode of treatment for sacrococcygeal teratoma. In neonates every attempt should be made tom remove the completely within the first week of life. After removal of the tumour the levator anatomy is reconstructed by suturing the rectum to presacral fascia.

In older children there is higher incidence of malignancy and the survival rate decreases. Only 45% of patients older than 2 years of age at diagnosis survived long term in one series.[6]

Finally it is well known that in rare cases, an unequivocally benign sacrococcygeal teratoma can recur as a malignancy after a successful removal. This occurs in about 3 – 10% of cases and is usually noted 6 – 33 months after initial removal.[6]

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Longstanding neglected foreign body in the nose

K.Jeet Singh, Talib Khan M.Lateef, Sajad Qazi, Shaqul Qamar

Abstract

Foreign bodies in nasal cavity in not uncommon problem usually in pediatrics age group. But here we present a case report in which unusual type of vegetative foreign body had been left in nasal cavity neglected for 20 years.

JK-Practitioner 2006;13(1):7-38

Case report:

A 35 years old normotensive lunatic male, with no history of bleeding diasthesis, fever, Jaundice, from hilly area presented with complaints unilateral headache and nasal obstruction for last 20 years with occasional foul smelling discharge and epistaxis. For the above complaints patient used to go to local physicians, quacks, Hakims, who used to give him antibiotics, nasal drops (decongestants), Treatment for migraine, antiallergic treatment providing only temporarily relief. Patient one day landed up in our ENT Department with above complaints.

On Anterior rinoscopy there was DNS towards right side with red inflamed area in the post part pus trickling and small ooze of blood below the inferior chonae. On Posterior rinoscopy there could be seen big mass with inflamed mucosa over it and pus and small ooze of blood on left side of nasal septum, filling whole of inferior meatus along the floor in the posterior part. Patient was admitted, all baseline investigations were done, were normal; culture sensitivity of discharging swab was also done which showed growth of stap epidermids, stap Aures, psodomonas which were sensitive to ciprofloxacin, and many other antibiotics. Patient was shifted to OT, GA given with ET intubation. Fibro-optic rigid endoscope was introduced in left nasal cavity, the mass present in the posterior part manipulated was hard in consistency, and was removed by pushing it backward into the nasopharynx- inferior tubrniate was necrosed in the posterior part which was also removed there was hemorrhage from the bed of rhinolith. The area was cleaned by betadine swabs and nasal packing was done. Antibiotics was given for 7 days in post operative period after cleaning the rhinolith unusual type of vegetative, FB body was found – Fig. (1). The post operative period was uneventful and relieved the patient of symptoms.

Discussion:

Foreign body in nasal cavity is not uncommon especially in peadeatric age group [1-6] Lunatics may thrust strange substances into their nostrils [1-4] Majority of the foreign bodies are vegetative in nature [1,2,6] as in our case though animate FB, and pebbles are also found. FB can enter into nose through anterior nares (common), post nares, penetrating wounds palatal perforation (Cleft palate), sequestration of bone insitu after trauma, calcification in situ [1,2,3,6,7] which in our case has been insertion through anterior nares.

Foreign body in the nasal cavity usually present with unilateral nasal obstruction and foul smelling discharge [1,3] and epistaxis. A few

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Abbreviations :

Foreign Body : FB.
Anterior Rhinoscopy : A R
Ear, Nose & Throat : E.N.T
General Anaesthesia : GA
Local Anaesthesia : LA
Deviated Nasal Septum : DNS
Posterior Rhynoscopy : P R
Operation Theatre : OT
Endotracheal Intubation : ETI

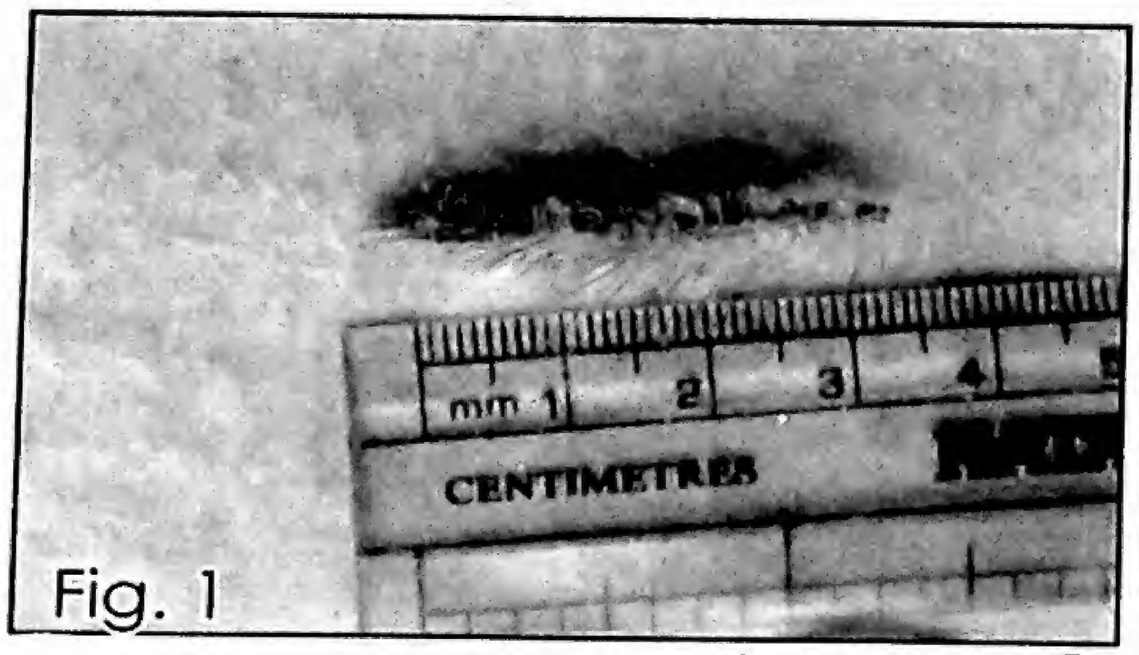

Fig. 1

foreign bodies are inert and give either no symptoms or unilateral nasal obstruction if large enough [1], or there may be a period of tolerance after introduction which may extend from few days to ten or more years [3] compared to 20 years in our in our case. But in child tolerance is soon established and incident is forgotten [3,7]. During this period it may produce one sided excess discharge very much aggravated at times when it becomes foul smelling and blood stained [3] similar to our case.

On A/R the foreign bodies can be seen or missed of surrounding edema or granulation tissue [1,3], similar to our case. In our case P/R has shown edema, granulation tissue over foreign body filling the posterior part of the inferior meatus along floor, as also mentioned in [1,3].

Foreign bodies can be removed under GA or LA depending upon size of FB, location of FB, condition of patient, duration of FB.

If foreign body is located posteriorly for long time it can be pushed in to the pharynx with proper precautions not to allow it to fall into esophagus and bronchus then removed [1,3,6] and same has been done in our case.

Also there have been the unusual cases like one mentioned by Guthrie [8] in which foreign body remain asymptomatic for long period 16 years and 17 years respectively, and were discovered incidentally as compared to our case in which FB stayed neglected 20 years.

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Neurofibromatosis type 2 (NF2) :A rare cause of teenage deafness

Manzoor Latoo, Lateef Mohammed, Rafiq Ahmed, Rouf Ahmed, Qazi Sajad. Nassima Chanda, Farah Sameem, Syed Besina

Abstract

Type 2 neurofibromatosis is a rare cause of deafness and tinnitus in the teenage It is an autosomal dominant disorder characterised by development of bilateral vestibular schwannomas in the second and third decade of life. We present a case of a 12 year old boy who presented with tinnitus and deafness with posterior lenticular opacity. MRI revealed bilateral vestibular schwannoma and meningioma of ventricular horn.

JK-Practitioner 2006;13(1):39-40

INTRODUCTION:

Type 2 neurofibromatosis (central or bilateral neurofibromatosis) is an autosomal dominant genetic disease characterised by development of bilateral vestibular schwannoma~ in second and third decade of life. It has been shown to be due to loss of tumor suppressor gene which has recently been cloned on chromosome 22q[1] .Fifty percent of the affected individual offsprings are likely to inherit this disorder. The national institute of health has led following diagnostic criteria for NF2[2].

Bilateral vestibular schwannoma or family history of NF[2].

Plus

1. Unilateral acoustic or

2. Any two of ; meningioma, glioma, neurofibroma, Posterior subcapsular lenticular opacity.

Case summary:

We present a12 year old boy a student of 8th primary a product of normal full term delivery with six year history of blindness right eye which initially began as dimunition of vision, progressed gradually and finally he was not able to see with his right eye. Patient also has 2 year's history of tinnitus which was felt as ringing sensation in right ear, prominent during night. Patient also gives two and a half months history of decreased hearing on the right side. There is no history of vertigo, ear discharge, headache, convulsion, fever, vomiting, weakness of any part of face, paresthesias, numbness. There was no complaint pertaining to any other organ system. There was no such history in the family. There were no audiological symptoms in the first degree family members.

Examination revealed inability of the patient to hear normal conversation. Right side eye had opacity in the pupil (Figure 1). There was one cafe-au-lait spot at the angle of the mandible on right side.

Ear examination revealed intact tympanic membrane which was dull lustreless with myringosclerosis. Left tympanic membrane was intact with normal cone of light. Tuning fork tests showed right sided sensorineural deafness. All cranial nerves were normal. There was no other skin lesion. Cold calorie test did not show any response on the right side . Pure tone audiogram showed right sided sensorineural hearing loss. Ophthalmologic examination was done which reported as right hypermature cataract with vision of 6/18 in left eye, no projection of light in the right eye and heterochromia.

With this clinical picture a tentative impression of NF2 was made. Patient was advised MRI brain, C P angle and spine. MRI showed an irregular hypointense lesion on T1w images in right CP angle with compression of the ipsilateral cerebellar hemisphere and mass effect on the 4th ventricle. The lesion was hyperintense on the T2w sequence. Also a small irregular hyperintense lesion was seen in the left CP angle with no mass effect or edema. Another well defined lesion was seen in the right frontal horn of right lateral ventricle. The radiological impression was that of .bilateral CP angle .tumor

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Key words: *Neurofibromatosis type 2, Posterior lenticular opacity, Café-au-lait spots, Deafness, NF 2.*

Fig 1

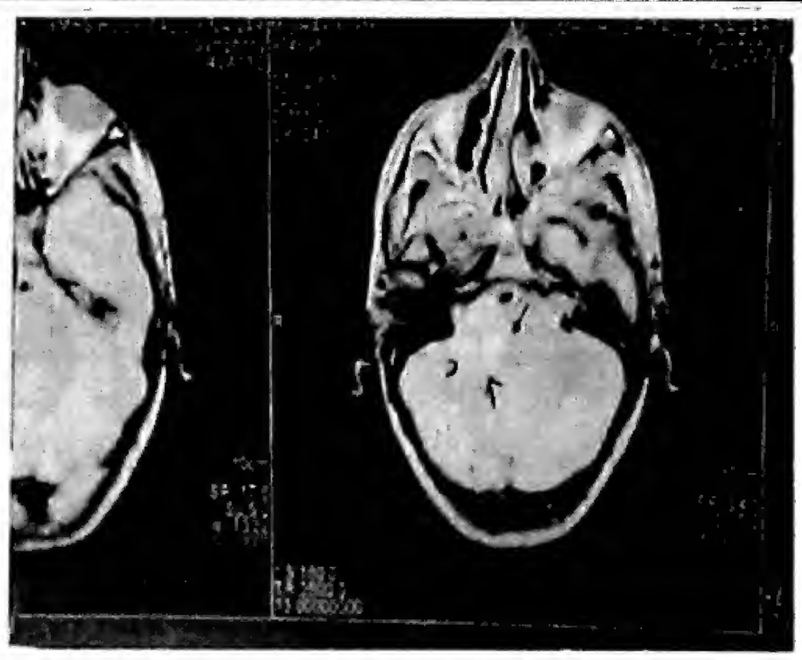

Fig 2

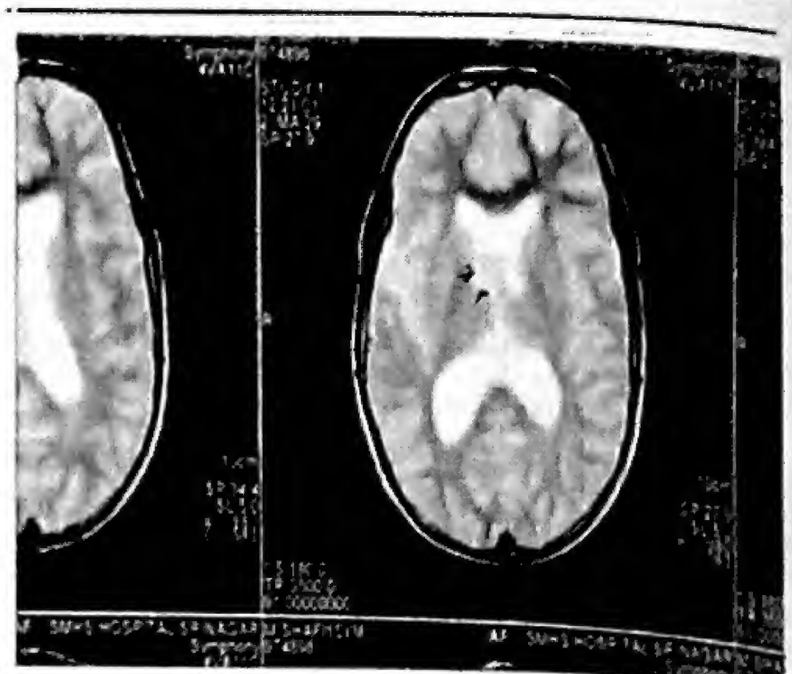

Fig 3

with intraventricular lesion(figure 2&3). Thus patient was filling the diagnostic criteria of the neurofibromatosis 2 as laid by the NIH 1987[2]. Patient was operated for the acoustic neuroma right and is being followed in the neurosurgery department.

Discussion: NF2 is a rare autosomal dominant disorder with a birth incidence of 1 in 35000 and actual diagnostic prevalence is only 1 in 200000.[3] Majority of cases of NF2 present with symptoms related to their vestibular schwannoma such as deafness tinnitus,imbalance or vertigo[4]. Most have unilateral symptoms at presentation but it is not uncommon for presence of silent second side tumor to be revealed during-the course. of investigation of an apparently unilateral problem. There is no predictable relationship between tumor size and degree of hearing loss. It is not uncommon to find a small tumor with poor hearing on one side and a contralateral large tumor with good hearing.

While assessing a teenager with audiological symptoms and keeping in mind all common causes, NF2 is also to be born in mind because it is rare but it is there. A clinical pattern in the form of unilateral tinnitus, hearing loss, vertigo with no obvious history of any inflammatory pathology in the past plus examination not in favour of any inflammatory pathology demands evaluation for acoustic neuroma and in a teenager for NF2. ;

Same clinical judgement has proved fruitful in our case where in a young boy of 12 year's with progressive hearing loss and decreased vision with no prevjous history of inflammatory pathology and examination also not in favour of any inflammatory pathology was suspected of having NF2.

Audiological assessment is important in arriving at diagnosis of NF2 as it might reveal mild to severe SNHL, a speech discrimination score lower than would be anticipated from the pure tone test, a low SISI score, partial or complete tohe decay and a type iii or iv Beksey audiogram and no recruitment.[4] However with the advent of MRI the diagnosis of NF2 has been revolutionised and in fact the audiological battery of tests is now longer a prerequisite . MRI with gadolinium enhancement has broadened our .knowledge of diverse and distinct CNS manifestations of neurofibromatosis. MRI is better than CT in detecting and defining many brain and spine lesions.[3]

In our case also pure-tone audiogram revealed severe SNHL , but instead of subjecting the patient to audiological battery of tests and being confident of clinical judgement we subjected patient to MRI and confirmed diagnosis.

Conclusion: We coclude that NF2 is a rare cause of hearing toss but it is to be kept in mind in a particular clinical setting and audiological battery is no longer a prerequisite with the advent of newer imaging modalities.

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MACRODYSTROPHIA LIPOMATOSA - A letter to the editor

Shiblee Hafeez, Masarat Syed, Arif Syed

A 14 year old girl presented with painless swelling of first and second toes of her right foot. Digits were slightly enlarged since birth and had continued to grow since then. There was no history of antecedent trauma. On examination, affected toes were found to be enlarged. Skin over digits was thickened, pale ,glossy and non tender. Consistency was firm in some areas and soft in others. Dorsal deviation of toes and plantar soft tissue hypertrophy was also noted. None of her family members nor she had neurocutaneous manifestations of neurofibromatosis.

X-ray of her right foot showed massive increase in size of 1st and 2nd toes with both bony and soft tissue overgrowth. Soft tissue growth was more marked on volar aspect with multiple translucencies. Other toes were normal Color Doppler examination showed abnormal vessels in local area.

After cosmetic surgery, histopathology of specimen showed massive increase in adipose tissue interspersed in a fine mesh of fibrous tissue involving subcutaneous tissues, bone marrow, periosteum muscle and nerve sheaths. No neural enlargement was seen. These findings were consistent with Macrodystrophia Lipomatosa.

Macrodystrophia Lipomatosa is an unusual form of local hypertrophy also called local gigantism . It is congential in origin but not hereditary [1,2]. It is classified as a developmental anomaly. There is marked increase in all mesenchymal elements i.e. bone, tendons, nerves and vessels but particularly fibro adipose tissue.

The rate of accelerated growth varies among patients and may vary among affected digits [3]. Its involvement is almost always unilateral as in our case but bilateralism is not rare. Lower limb is more frequently involved than upper limbs. The most common sites are 2nd and 3rd digits. Fifth digit involvement is rare. Soft tissue overgrowth is most marked at distal end and volar aspect of the digit. Volar overgrowth produces dorsal deviation and splaying of digits with endosteal &periosteal bone deposit. Growth of the digits ceases at puberty. High incidence of syndactyl ,polydactly and clinodactly is present with slanting of articular surface

Patient usually seeks surgical correction for cosmetic reasons. Mechanical problems due to secondary degenerative disease or neurovascular compression may occur late in childhood or adolescence.Carpal tunnel syndrome can occur [4].

Exact etiopathogenesis [1,2] is obscure. Proposed mechanism include lipomatous degeneration, disturbed foetal circulatioin. disturbances of growth inhibiting factors, an error in segmentation. trophic influence of tumefied nerve. Ingles and others have postulated that this anomaly could be an expression of neurofibromatosis, but contradictory views have been expressed by many authors based on following observations:(i) lack of neurocutaneous or other systemic abnormalilties in patients with macrodystrophia. (ii) absence of increased incidence of local gigantism or other anomalies in family members (iii) sporadic presence of neural enlargement which is the result of fibrosis of sheath rather than neural tumefaction (iv) a disproportionate increase in adipose tissue (v) differences in radiographic features [5]

Radiological D/D of macrodystrophia includes both congenital and acquired disorders. Congenital anomalies include conditions like- hyperostotic macrodactyly (increase in all mesenchymal elements), haemangioma,lmphangioma (only soft tissue overgrowth in both). Olliers

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Fig.1 : AP view Showing massive soft tissue as well as bony overgrowth

Fig.2 Lateral view : Shows soft tissue overgrowth predominantly on the volar aspect with splaying & dorsal deviation of toes

disease (enchondromas), Klippel-Weber-Trenauny syndrome (Haemangiomas and macrodactyly), plexiform neurofibromatosis, melorheostosis (increased bone density with candle wax dropping periosteal reactions).Acquired conditions like-infarction, infection, trauma, JRA can be eliminated by history.

Amongst the above, most difficult to eliminate is neurofibromatosis , where enlarged digits may be bilateral and the distal phalanges are not the most severely affected. Mere macrodactyly is the result of plexiform neurofibromatosis but haemangiomatous and lymphamgiomatous element can produced premature fusion of the growth plate. Soft tissue lucencies are absent. '.

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Effect of *Tamarix gallica* Leaves on Experimental Liver Cell Injury.

Tabassum N, Chatturvedi S, Agrawal S.S

Abstract

50% ethanolic extract of dried leaves of *Tamarix gallica* (TG), commonly known as Jhavuka in Hindi, was screened for antihepatotoxic activity against acetaminophen induced hepatocellular damage in albino mice. Acetaminophen produced hepatotoxicity in mice as evidenced by degenerative changes, focal necrosis and sinusoidal dilatation in the livers. Tamarix gallica extract when administered at different doses revealed presence of binucleated cells, anisonucleosis and anisocytosis in all the extract treated groups of mice.

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Introduction:

Tamarix gallica (TG) (Fam: Tamaricaceae) is a gregarious bushy shrub that grows on saline or water logged soils [1,2]. It is a component of marketed hepatoprotective combination Liv-52[3]. The principle constituents are tamarixin along with traces of its aglycon, tamarixetin[4]. It is used in bleeding disorders like menorrhagia, bleeding in the rectum and epistaxis[5]. It is also used in disorders associated with hepatic insufficiency and has a salutary effect on liver glycogen and proteins[6]. Leaves of TG have been reported to be useful in hepatic and splenic disorders[7].

The present paper deals with the antihepatotoxic activity of 50% ethanolic extract of TG leaves at different doses (25, 50 & 100 mg/100g/day) against acetaminophen induced hepatocellular damage.

Material and methods:

Leaves of TG were extracted with 50% ethanol by cold maceration process as described in I.P 1985 [8]. Healthy albino mice (20-35g) of either sex were used in the study and were divided into five groups of 8 mice each. Group I served as control and received 1ml of 1% gum acacia suspension. Group II received a single oral dose of acetaminophen, as a supersaturated solution in 0.9% saline at the rate of 500mg/kg body weight[9]. Groups III, IV and V received 25, 50 and 100 mg/100g/day of TG extract respectively for five days, after 48 hrs.of acetaminophen administration. Blood was withdrawn, 24 hrs. after the administration of the last dose of the drug and the serum was subjected to Serum Glutamic Pyruvic Transaminase (SGPT/ALT) estimations [10]

The animals were sacrificed and their livers were subjected to histopathological studies using Haematoxylin Eosin (H & E) stain.

Results:

The ALT levels were significantly increased by acetaminophen administration in mice of Group II. Histopathological studies revealed large areas of necrosis in 67 % animals, surrounded in focal distribution, lymphocytes and lot of haemosiderin pigment.

Mice treated with 50% ethanolic extract of TG at the dose of 25mg/100g revealed binucleated cells, anisonucleosis and regenerative changes. Slight regeneration, sinusoidal dilatation, mild anisocytosis and few binucleated cells were however observed with TG at the dose of 50mg/100g b.w (Fig 1). Tamari .gallic at the dose of 100mg/100g b.w revealed sinusoidal dilatation, slight kupffer cell hyperplasia and regenerative activity with binucleated cells spread all over (Fig 2).

Discussion:

Acetaminophen induced hepatic liver cell damage was studied in

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Key words: *Acetaminophen, Tamarix gallica, antihepatotoxic.*

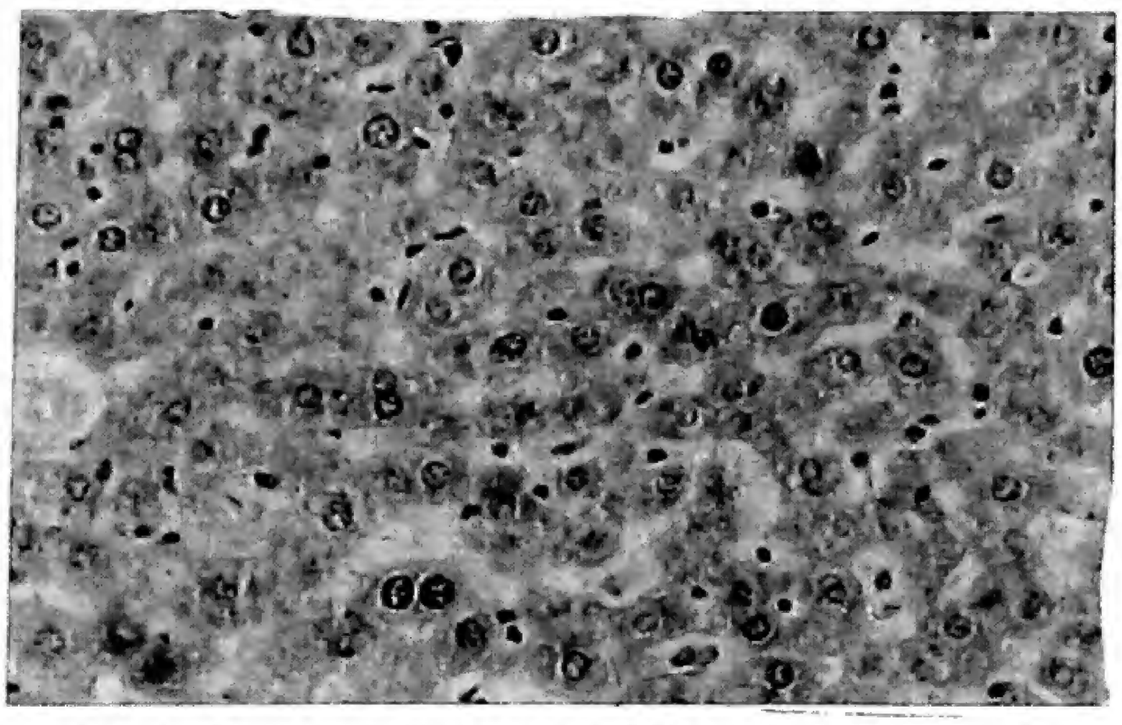

Fig.1 :Paracetamol + 50% Ethanolic Extract of *Tamarix gallica* (50mg/100g Body weight) Few Binucleated Cells (H & E x 400)

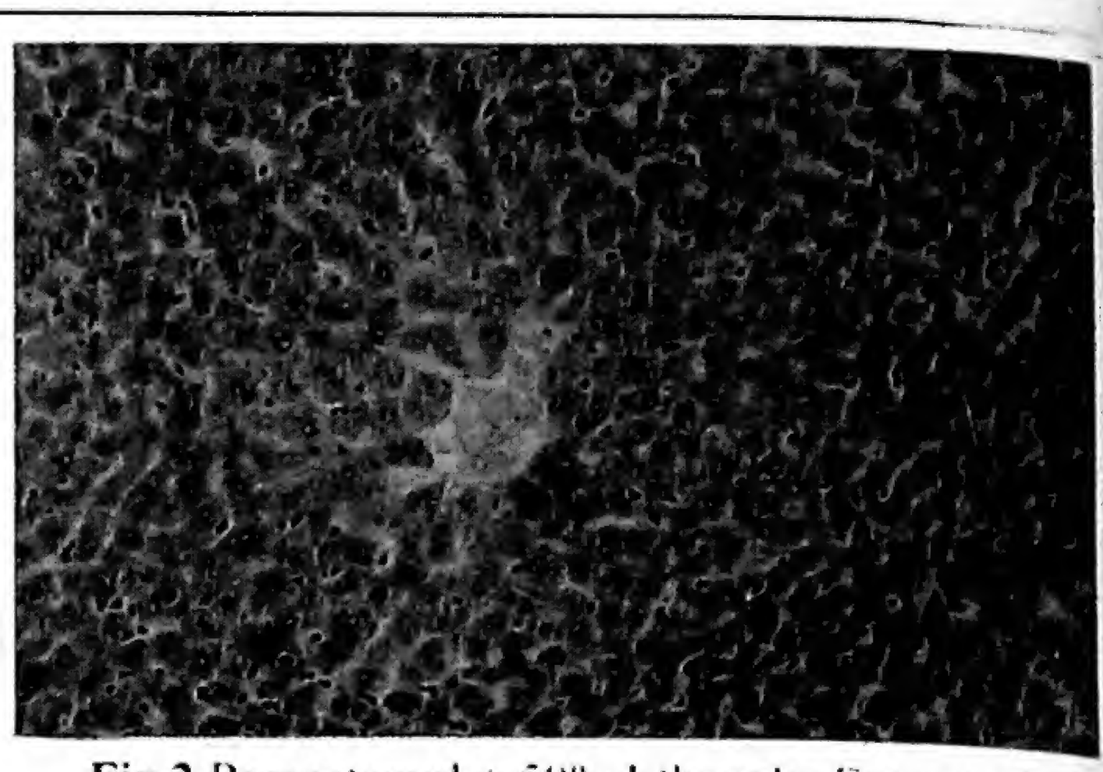

Fig.2 Paracetamol + 50% Ethanolic Extract of *Tamarix gallica* (100mg/100g Body weight) Binucleated Cells Spread all over (H & E x 400)

mice as its toxicity is maximum in mice [11-13]. The animals became very weak and their body weight was reduced considerably during one weak experimental study. However, with different doses of ethanolic extract of TG there was no reduction in body weight and food consumption. Animals looked quite healthy.

ALT was taken as an index for biochemical estimations as it is more abundant in liver cells than in any other cells in the body[14] Biochemical and histopathological studies revealed that paracetamol in a single oral dose of 500 mg/kg body weight is hepatotoxic in mice. 50% ethanolic extract of Tamarix gallica leaves showed evidence of antihepatotoxic activity in mice in this study but it was not dose dependent.

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Epidemiology Statistics regarding maternal mortality rate (Post caesarlan)

Tabassum Parvez, Yasmeen Wani

Caesarian section are under taken in 5 to 13 % of labours. According to DC Dutta studies on Indian women showed that maternal death should not exceed 2 per 1000 caesarian. But with adverse patient profile and not too good circumstances, which are most common interrelated, maternal mortality ranges from 0.5 to 3%.

Maternal mortality is death occurring during pregnancy and 42 days later.

Accepted figures are:

1. In developing countries 4 per 1000 live births.
2. in India 300 / 100,000 live births.

Magnitude of problem:

1. Out of estimated half million annual maternal deaths in the globe. 99% are distributed in the developing countries.
2. Shocking scenario revealed one maternal death per minute in developing countries.
3. For one maternal death at least 15 more suffer from severe morbidities.
4. More maternal deaths in India in a space of a week than in all of Europe in a whole year.

Causes of maternal death following caesarian section:

❖ **Immediate (occurring within 24 hours)**

- Immediate causes are hemorrhage and shock because of post-partum haemorrhage or internal leak. In haemorrhagic loss following caesarian section one litre of blood is lost. Exceeding this amount and without correcting pre-existing dehydration and ketoacidosis may lead to immediate cause of death.
- Anaesthetic hazard: Because of aspiration of gastric contents due to delayed stomach emptying leading to aspiration atelectasis or aspiration pneumonitis (Mendelson's syndrome). Other causes acute dilatation stomach post-operatively.
- Pulmonary embolism/ Thrombo embolism responsible for 15 to 25 % of maternal deaths in western countries. 2 to 5 % in India.
  - It is a very important factor of mortality as leg vein thrombus or uterine can lead to pulmonary embolism after reaching the right heart through venacava. Thrombus can be small, big or massive and sign and symptoms depend on the size of the thrombus.
  - **A small clot** passes to lung periphery and cause a wedge shaped infarct seen on X-ray. Chest pain usually present may be associated with moderate cyanosis and dyspnoea.
  - Later pleural rub and pleural effusion may occur. In this sign and symptoms are not necessarily impressive.
  - **In big clot** intense chest pain acute dyspnoea and cyanosis occurs with immediate development of shock and whole lung is involved. Picture is dramatic and compelling. ECG shows right ventricular strain, right axis deviation or RBBB.
  - **In massive thrombus** obstructing bifurcation of pulmonary artery, no pulse is felt and Ashen grey pallor of shock is seen.
  - Other causes related are: Amniotic fluid embolism, through uterine sinuses.
  - Air embolism via intravenous infusion.

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- Or already pre-existing cardiac ailment like myocardial infarction which may be aggravated post operatively.

❖ **Delayed (occurring after 24 hours)**
Sepsis following caesarian section in labour or in premature rupture of membrane. Other sites of infection are abdominal wound, uterus or peritoneal cavity (peritonitis).

❖ Sudden causes of death following caesarian section:
- Big pulmonary embolus at bifurcation of pulmonary trunk.
- Amniotic fluid embolism.
- Acute myocardial infarction or cardiac arrest.

Symptoms of deterioration before death:
Because of small pulmonary embolism or amniotic fluid embolism can be chest pain, dyspnoea, sweating with mild or no cyanosis.

Anesthetic Risks: Anesthetic mortality is about 0.05%; death in the recovery period is about 0.1% and 0.6% occurs in the first post-operative week. Anesthesia also contributes to 14% of all deaths. 50% of anaesthetic mortality death/morbidity (complications) is due to problems with ventilation i.e, problems in delivering oxygen to the patient; 30% is due to heart (cardiac) problems. The mortality incidence while in hospital is about 1% in healthy patients. This 1% incidence is increased in the presence of preexisting disease. The obstetric maternal mortality rate is now about 1 per 10,000; in the 1970's the rate was double. Some of these maternal deaths are due to general anaesthesia; however, the increased use of local anaesthesia (50% of caesarian section are currently performed under local anaesthesia) is probably reason for reduction of maternal mortality. The incidence of mortality and morbidity obviously also depends on the patient's with multiple medical problems (unknown and undiagnosed).

Amniotic Fluid Embolism:
- Can result from Amniotomy and strong uterine contractions.
- Seen to occur 90 minutes after LSCS upto 48 hours after delivery.
- Has been suggested to occur in 4 phases:
  - Release of amniotic fluid.
  - Pulmonary artery spasm.
  - Left ventricular and pulmonary capillary injury.
  - Left ventricular failure and ARDS.
- Mode of presentation:
  - 50% patients die within first hour rest 40 % will develop DIC or manifest bleeding from incision or vene puncture site.
  - May present with cyanosis, cardio pulmonary arrest, pulmonary edema or ARDS.

Nearly half of the global estimated annual 515,000 maternal deaths occur in sub-Sahara Africa. Nearly a quarter of these occur in the countries of UNICEF East and South Africa Region (ESAR). The high ratios of maternal mortality in African countries call for an intensified effort to reduce maternal deaths caused by obstetric complications which can be treated. The major direct causes of maternal deaths are unsafe abortion, hemorrhage, sepsis, pre-eclampsia and eclampsia, and obstructed and prolonged labour. The important indirect causes include HIV/AIDS, Malaria, TB and Malnutrition.

In its 55th session, the General Assembly adopted the UN Millennium Declaration, which resolved to reduce maternal mortality by 75% by the year 2015.

Techniques for measuring mortality: The ideal way to monitor maternal mortality is through vital registration. However, in most developing countries , vital registration suffers from two serious problems: first, many deaths are not recorded(under reporting),generally because they do not occur in health facilities; and second , many maternal deaths are misclassified. Even in developed countries, studies have shown that maternal deaths are misreported by 50% on average. Alternative methods, noted by Ms. Campbell, include:

Sisterhood method: This demographic technique uses surveys to ask women about the survival of their sisters. It requires relatively small sample sizes and is therefore comparatively inexpensive.

WHO/UNICEF models: These models are based on data from countries with relatively good data on maternal mortality; data on general fertility rate and the coverage of skilled attendant at delivery are used to generate an estimate of the countries maternal mortality ratio.

Ms Campbell concluded, unless a countries vital registration system is very good, maternal mortality should not be used as short term outcome indicator for safe motherhood programs.

Maternal mortality estimates can be used for the

following purposes:

- To gain a general sense of the size of the problem .
- To sensitize policy makers ,program planners, and others to the magnitude of the problem.
- To stimulate discussion and action and
- To mobilize national and international resources for maternal health.

Maternal mortality indicator:

Proportional maternal mortality: This figure represents ratio of number of maternal deaths among women of reproductive age. This shows how important maternal mortality is as a cause of death among women.

Very important to know that in almost half the cases the severity of women's condition was not recognized until more than 24 hours after the problem arose, reflecting a high threshold to pain and health problems and the belief that complications during pregnancy and delivery are normal, natural event.

UNICEF's top priority interventions are directed towards maternal mortality rate reduction: (a) supporting Govt. to provide high quality emergency obstetrics care (b) supporting Govt. to recruit ,train ,deploy ,and maintain health providers (c) supporting Govt. efforts to promote family planning and (d) assisting Govt. monitor programs through the UN process indicators.

WHO recently showed maternal mortality is one of the major public health problem challenging medical community especially in developing countries. It showed 5,80000 maternal deaths occurring annually, 99 of them in the developing world. *Maternal deaths account for less than 1% of deaths in women of reproductive age group in the developed world, but the corresponding figure for developing countries is close to 25 to 30%.* Maternal mortality is important not only it represents the single most preventable cause of deaths among women of reproductive age, but also it is an important contributing factor to infant and child mortality. Current maternal mortality estimates for Asia are 420/100,000.

Most mothers who died following caesarian section were caesarian performed for patients referred for obstructive labour from long distances.

Major causes of maternal deaths: Hemorrhage, Sepsis, Hypertension from the third world.

WHO estimates indicate that maternal mortality rate has in fact increased in the last 10 years from 500,000 to 580,000 deaths per year through out the developing world.

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Pregnancy in Women with Kidney Disease

Ghulam Hassan Malik, MD,DM,FISN,FACP; Masood ul Hassan, Malik Suhail,

A woman during pregnancy can develop any of the following renal problems-
Urinary tract infection,
Pre-eclampsia including HELLP(hemolysis,elevated liver enzymes,low platelets)syndrome,
Transient hypertension,
Acute renal failure,
Hemolytic uremic syndrome/thrombotic thrombocytopenic purpura
Acute fatty liver of pregnancy.
These conditions will not be considered in the present review since these complications arise when a woman without any underlying kidney disease becomes pregnanct.

The present review will discuss the problems when a women with underlying kidney disease becomes pregnant.
The subject has to be viewed from two aspects:
a)The effect of pregnancy on the kidney disease and
b)The effect of the kidney disease on the outcome of pregnancy.

The subject will be discussed under the following headings:
1)Renal functional and structural changes during pregnancy
2)Chronic renal disease
3)Diabetic nephropathy
4)Renal transplant reciepents
5)Systemic lupus erythematosus(lupus nephritis)

Renal functional changes during pregnancy:

Significant changes in renal function occur during pregnancy.Renal plasma flow increases to 50% -70% above normal in first two trimesters and remains 40% above normal in the third trimester.The increase in renal blood flow is due to an increase in cardiac output and decrease in renal vascular resistance as a result of renal vasodilatation.In contrast to the large increase in renal blood flow,there is no increase in cerebal or hepatic blood flow during pregnancy.An increase in glomerular filtration rate(GFR)begins by the fourth week of gestation and is 50% above normal by 13 weeks.Blood pressure and peripheral vascular resistance fall soon after conception.The fall in vascular resistance is thought to be due to increased synthesis of vasodilating prostaglandins(prostacyclin)

The average *BUN* for pregnancy is9mg/dL(N=10-20mg/dL) and the average serum creatinine is 0.7mg/dl(N<1.5mg/dL).A *BUN* of 14mg/dL or creatinine above 0.9mg/dL is indicative of abnormal renal function.The increased GFR leads to increased clearance of uric acid and a decrease in serum uric acid level.GFR also varies with position being 20% lower in the supine compared to lateral position.

Tubular functions also change with changes in glomerular function.A 50% increase in GFR during pregnancy necessitates an equal increase in sodium reabsorbition by the renal tubules.The osmostat is reset and thirst is experienced at a level 5mOsm below the non- pregnant state and serum sodium is 5mEq/l below nonpregnant normal.The threshold for glucose reabsorbtion increases and glucosuria may be noted without hyperglycemia.

Anatomical Changes:

Anatomical changes in kidneys also occur during

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pregnancy.Renal length increases by 1-1.5 cm due to increase in vascular volume and capacity of collecting system and hypertrophy.Dilatation of renal collecting system(physiological hydronephrosis)more often on the right side occurs due to hormonal changes(also known after oral contraceptives)as well as due to mechanical factors.The dilatation begins in the first trimester and lasts upto 12 weeks postpartum.

Chronic Renal disease in pregnancy:

In women with renal disease there are several considerations of the interaction between renal disease and pregnancy .Renal disease can have serious consequences for both maternal health and fetal outcome.On the contrary pregnancy can have adverse effect on renal function which may or may not be reversible.Any pregnant women with an underlying renal disease should be managed jointly by an obstetrician experienced in high risk pregnancies and by a nephrologist

Hypertension:

Hypretension is common in kidney disease more often with glomerulonephritis.It can be seen even in the absence of renal insufficiency.Treatment of hypertension during pregnancy is similar to chronic hypertension.Women with renal disease and hypertension are at increased risk for superimposed preeclampsia and its diagnosis becomes difficult.Proteinuria due to underlying renal disease worsens and serum uric acid may also increase due to decrease in GFR.Two parameters are helpful in this situation-worsening of hypertension and hyperreflexia both of which favour preeclampsia.HELLP syndrome is an advanced stage of preeclampsia and easy to diagnose.If hypertension becomes difficult to control termination of pregnancy is usually needed.

Proteinuria:

Proteinuria due to renal disease increases during pregnancy.Nephrotic range proteinuria may occur particularly in glomerulonephritis.Increased proteinuria is due to increase in GFR and increased filtered load of protein.Heavy proteinuria itself is not associated with hypertension or worsening renal function.Salt restriction is needed if heavy proteinuria develops.

<u>Pregnancy in women with renal disease and normal renal function</u>

In general if renal function is normal at conception.it does not worsen during pregnancy.A transient decline in renal function,hypertension and increase in proteinuria may be noted.The rate of live births remains above 90% if blood pressure is well-controlled.

In a study of 360 women with glomerulonephritis and normal renal function,170 became pregnant (others did not and served as control).On follow up of upto 30 years no difference in renal survival was noted.However,patients with hypertension had more progressive renal disease[2].

In a study of repeated pregnancies in Membranous glomerulonephritis(MGN) including patients with 2 or more pregnancies .51 pregnancies were noted in 9 patients ranging 2-12(average 5.6).Thirty pregnancies were noted after MGN ranging 2-5(average 3.2)and duration of follow up was upto 10 years.Comparing the pregnancy outcome-full term, preterm(delivery before 37 weeks),live birth,abortion,perinatal mortality,low birth weight and cesarean section there was no statistically significant difference between the pregnancies which occurred before and after MGN. Comparing the first and last pregnancy after MGN there was no statistically significant difference in hypertension, proteinuria and serum creatinine levels.One patient underwent 5 pregnancies and serum creatinine after followup for 6 years was 2.5mg/dl.The conclusion was that the outcome of pregnancy was good with 90% live births and that repeated pregnancies do not influence the course of MGN[3]

In another study of repeated (2 or more)pregnancies in 17 women with Non- Immunoglogin A Mesangioproliferative GN(Mes GN) 135 pregnancies were noted and 85 pregnancies were post Mes GN.The number of pregnancies ranged from 2 to 11(mean 5)and were followed upto 20 years.Comparing the outcome of the 50 pre and 85 post Mes GN pregnancies a higher frequency of low birth weight,cesarean sections and pre-eclampsia was noted in the post Mes GN group.However low birth weight and cesarean section of the post Mes GN group was comparable to the normal deliveries.Comparing hypertension, proteinuria and serum creatinine between the first and last pregnancies of the post Mes GN group there was no significant difference.Only 2 developed renal impairment on last follow up –one underwent 5 pregnancies all full term over 9 years and the other 11 pregnancies (all full term)over 20 years.The conclusion was that outcome of repeated pregnancies in Mes GN was comparable to normal deliveries,a higher frequency of pre-eclampsia,low birth weight and cesarean section was noted in post compared to pre Mes GN pregnancies. Repeated pregnancies did not influence the course of Mes GN[4]

Renal biopsy during pregnancy

Indications for renal biopsy during pregnancy are few-sudden unexplained deterioration in renal functio.Blood pressure should be well maintained and coagulation profile normal.After 32 weeks biopsy is not recommended[5].

Pregnancy in women with Chronic Renal Failure(CRF)

The outcome may be very different in women with moderate renal insufficiency(plasma creatnine 1.5-1.9 mg/dL). In this setting the plasma creatinine tends to decline slightly during the first half of pregnancy (as in pregnancy in women without kidney disease) and then increases above the pre- pregnancy base line[6]. Upto one

third may have irreversible decline in GFR and it may exceed 50% if uncontrolled hypertension is present.[7] Worsening of renal function was more common in women who had hypertension during the third trimester.A greater degree of renal insufficiency at conception was associated with acceleration of disease during pregnancy..

Prematurity ,preterm delivery and growth retardation are more common compared to normal pregnancies.Overall fetal survival is lower.

Pregnancy in dialysis patients

Infertility is the rule in dialysis patients. Pregnancy is uncommon with a reported frequency of 0.3 to1.5%. Pregnancy is accompanied by worsening anemia.Hypertension can be a life threatening complication.Sucessful outcome has been noted in 40-50%.

Problems and recommendations:

Hypertension needs an aggressive management.Dialysis should be intensified to keep *BUN* below 50mg/dl to avoid hydramnios and improve nutrition. To treat anaemia higher doses of Erythropoietin are needed to keep Hb above 10g/dl.Metabolic acidosis and hypocalcemia need to be corrected.Careful uterine and fetal monitoring is required.Hypotension during hemodialysis is to be avoided.20% pregnancies are lost due to second trimester abortions.Pre-term delivery is almost a rule(mean gestational age of 30.5 weeks).

Diabetic Nephropathy

Diabetic nephropathy is characterized by proteinuria, hypertension and reduced glomerular filtration. A diagnosis of diabetic nephropathy is made if there is persistent proteinuria of more than 300mg/day in first 20 weeks of pregnancy.

Effect of pregnancy on Diabetic Nephropathy:

Proteinuria increases during pregnancy and regresses after delivery.The effect of pregnancy on diabetic nephropathy depends on renal function at the time of conception like other renal diseases.Pregnancy does not accelerate the progression of nephropathy with normal or mildly impaired renal function.

Women with moderate to severe renal insufficiency show a rise in serum creatinine by third trimester that may persist post-partum. 11 women with diabetic nephropathy and serum creatinine more than 1.5mg/dl had accelerated progression of renal failure compared to control group[8].

Effect of Diabetic Nephropathy on Pregnancy

Diabetic nephropathy is associated with pregnancy complications such as increased frequency of intrauterine growth retardation, fetal distress and pre-eclampsia .Pre- term deliveries and cesarean section are often needed.

Management Principles:

1) Pre-conception: Evaluation of proteinuria/day and creatinine clearance are essential. The angiotensin converting enzyme(ACE) inhibitors need to be changed to other antihypertensives.

2) Hypertension: Strict blood pressure control is needed (below 130/85mmHg). ACE inhibitors and angiotensin receptor blockers are contraindicated.

3) Pre-eclampsia: Proteinuria and edema increase by third trimester. It may be difficult to diagnose but worsening of hypertension is suggestive of preeclampsia.Delivery is the definitive treatment for pre-eclampsia.Delivery is also undertaken in presence of abruptio,fetal growth retardation and distress. Low dose aspirin may be used but it is controversial

Pregnancy in Renal Transplant Recipients

Fertility returns after renal transplantation.More than 6000 pregnancies have been reported in renal transplant recipients till 1998.In general pregnancy is advisable after one year in live related donor recipients or 2 years after cadaver transplant.Pregnancy can be undertaken if serum creatinine is less than 2mg since there is substantial risk of worsening of renal function or of graft loss with more than 2mg/dl at conception.

The conditions which favour a successful outcome of pregnancy are:

1) Absence of hypertension.
2) Mild proteinuria.
3) Absence of graft rejection.
4) Minimal immunosuppression.

Causes of impairment of renal function during pregnancy are similar to the non pregnant recipient as follows:

1:Cyclosporin/Tacrolimus toxicity.
2:Acute Rejection.
3:Obstructive uropathy
4:Recurrence of primary disease
5:Pre-eclampsia
6:Pregnancy related causes of acute renal failure.

Delivery:

Vaginal delivery is encouraged as renal allograft does not obstruct the birth canal.Cesarean section is advisable only for obstetric reasons.Prophylactic antibiotics are advisable.

Fetal outcome is successful in 92% cases.

Medications:

Cyclosporin:Dose needs to be adjusted-generally2-4mg/kg/day.Metabolism increases during pregnancy and higher doses than pre- pregnancy may be needed.It is not a major teratogen

Tacrolimus:In a study of 100 pregnancies reported in 84 patients on Tacrolimus(27% renal transplant recipients)68 were live births with 60% premature[9].

Prednisolone: Pregnancy is recommended if prednisolone dose is less than 15mg/day.Maternal blood levels are 10 times higher than the cord blood. However adrenal insufficiency may occur in the infant.High dose steroids during pregnancy are safe in treatment of rejection.

Azathioprine: Frequency of congenital anomalies is sightly increased if at all.Fetal leucopenia is minimized if maternal leucocyte count remains normal.

Mycophenolate Mofetil: Adverse effects on fetal development have been observed in experimental animals and is contraindicated.

Sirolimus: Sirolimus is contraindicated.Its therapy should be discontinued at least 6 weeks before pregnancy and switched to cyclospoprin.

Pregnancy in women with Lupus Nephritis

SLE is frequent(female:male=9:1) in women of childbearing age.Prognosis for mother and fetus is best when the disorder has been quiescent for at least 6 months and renal function is adequate..

Pregnancy in women with lupus nephritis is associated with an increased risk of fetal loss (up to 25 percent) and with worsening of the renal and extrarenal manifestations . . These problems can occur during pregnancy and are more common in the first eight weeks postpartum. Patients with anticardiolipin antibodies and the lupus anticoagulant are at increased risk; and all pregnant women with lupus should be screened for lupus anticoagulant activity[10,11]

The frequency of exacerbation varies with the state of disease activity, ranging from 7 to 33 percent in women who have been in remission for at least six months and from 61 to 67 percent in women who have active disease at the time of conception [10,11] It is not clear, however, if these disease flares are due to pregnancy per se.

Although the incidence is not high, severe renal exacerbations can occur . As a result, women with lupus nephritis should be encouraged to delay pregnancy until the disease can be rendered inactive for at least six months. The negative prognostic implications of preexisting hypertension and azotemia in pregnancy also apply to lupus patients. It has also been suggested, although not proven, that the frequency of postpartum flares can be diminished by increasing the corticosteroid dose for four to five days after delivery .

Treatment of active lupus nephritis in the postpartum period is similar to that in other patients with this disorder. Oral prednisolone (30 to 60 mg/day) is usually used, although there is a risk of inducing or exacerbating hypertension, gestational diabetes, and premature rupture of membranes .. Cyclophosphamide should be avoided if possible during pregnancy, but azathioprine can be used with relative safety as long as the white blood cell count is normal.

Obstetric management of women with underlying renal disease

Close follow up by Nephrologist and Obstetrician is needed.The general principles are:

1) *Increased frequency of prenatal visits:every 2 weeks in first 2 semesters and weekly thereafter*
2) *Serial monitoring (monthly) of renal function.*
3) *Monitoring for pre-eclampsia.*
4) *Fetal surveillance (ultrasonography and fetal heart monitoring)*
5) *Treatment of hypertension.*
6) *Timing of delivery (preterm intervention in presence of deteriorating renal function,severe pre-eclampsia,fetal growth retardation or distress).*

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Commonly encountered reproductive tract infections in women

Abida Ahmad

It has long been recognized that reproductive tract infections (RTI) form one of the most common problems in women during reproductive age group. The clinicians today have access to accurate tests for etiological diagnosis and are in a position to provide prompt appropriate treatment for RTI and prevent their long term health consequences. Depending on etiology the RTI's in women may be divided into:

1. Sexually transmitted diseases (65-70%), increasing globally.
2. Pyogenic infections following unsafe abortion and puerperal sepsis (15-20%).
3. Iatrogenic infections associated with D&C, IUCD insertion etc. (5-10%).
4. Rarely tuberculous infections, mainly blood borne from foci elsewhere like lungs and lymph nodes (5%).

Defence mechanisms against RTI

The female genital tract offers a continuous open pathway from exterior to the peritoneal cavity. This is essential to allow ovulation and fertilization to occur. Several effective defence mechanisms have been evolved by nature to prevent infections of genital tract and their upward spread. Some of those defence mechanisms are:

Vulva :

1. Its skin being vascular is inherently resistant to infections.
2. Undecyclenic acid rich secreations of apocrine glands on vulva act as fungicidal.
3. The apposition of labia protects the genital tract above.

Vagina:

1. Apposition of anterior and posterior walls keeps the vagina closed to external infections.
2. A well developed stratified squamous epithelium lines the vagina.
3. Presence of Doderleins Bacilli inhibits the growth of other organisms by lactic acid production that increases vaginal acidity.

Cervix:

It remains functionally closed by mucus plug which as well has a bacteriolytic activity.

Uterus:

Periodic shedding of surface endothelium tends to eliminate infection if any.

Certain factors that reduce the efficiency of these natural defence mechanisms are:

1. **Age**: Childhood and post-menopausal period:
   - A. Vaginal epithelium is thin with low glycogen content
   - b. Fewer Doderleins bacilli are present and PH reaches 7.
   - c. There is no cyclical shedding and reformation of endomertrium.
2. **During Menstruation**:
   - a. Cervical plug is absent.
   - b. Lower vaginal acidity because of menstrual discharge which is alkaline.
3. **During puerperium and post abortal period**
   - a. The placental site is raw.

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b. Epithelial lining of cervix and vagina is broken.
c. The tissues are bruised and devitalized
d. Reduced vaginal acidity.
e. Wide open vulva, vagina and cerxix.
f. Lochia offers an excellent medium for organisms to grow.

In addition to the above mentioned factors anaemia, undernourishment, poor menstrual hygiene, lack of asepsis during delivery and unsafe abortions increase the risk of reproductive tract infections (RTI) in developing countries.

RTI can be grouped into upper and lower RTI. Lower RTI includes vulvovaginitis and cervicitis whereas upper RTI includes pelvic inflammatory disease or PID which in turn includes endometritis, salpIngitis,, oopheritis and sometimes pelvic peritonitis as well. Lower RTI shall be discussed in this issue.

1. **Vulvo vaginitis:** Valvovaginitis is an extremely common syndrome. More than 25% women attend Gynaec. OPD with symptoms related to vulvovaginitis. 75% of all women experience at least one episode of vulvovaginal condidiasis during their life time. Use of antibiotics, elevated levels of estrogen, sexually active life style and history of sexually transmitted diseases increases the occurrence of vulvovaginitis. The symptoms include vulvar irritation, dysuria, vaginal discharge with or without odour and labial erythema. Laboratory findings show a change in vaginal PH. Microscopic examination of vaginal secreations may show characteristic yeast forms, clue cells or trichomonads.

Bacterial vaginosis:

Epidemiology: Bacterial vaginosis (BV) is the most common causes of vaginitis in women of child bearing age. It has been diagnosed in 17-19% of women seeking gynaecologic care in family practice. The prevalence increases to 24-37% in women attending STD clinics. It has been observed in 16-29% of pregnant women. Gardnerella vaginallis has been found in 10-31% of virgin adolescent girls but is found more frequently among sexually active women reaching a prevalence of 50-60% in some at risk populations.

Pathogenesis and pathology: BV is a result of massive overgrowth of mixed flora, including peptostreptococci, bacteriodes spp, G. vaginalis, mobiluncus spp. and genital mycoplasma. There is little inflammation and the disorder represents a disturbance of vaginal microbial ecosystem rather than a true infection of tissues. The overgrowth of mixed flora is associated with a loss of the normal lactobacillus spp. dominated vaginal flora.

Clinical features and diagnosis: Upto 50% of patients of BV may be asymptomatic. An abnormal vaginal discharge, malodourous, fishy and infrequently profuse may be seen. Pruritis, dysuria and dyspareuria are rare. Examination often reveals a non-viscous, grayish white adherent discharge. The clinical diagnosis of BV can reliably be made in the presence of at least 3 of the following objective criteria.

- adherent, white, non floccular homogeneous discharge.
- Positive amine test, with release of fishy odour on addition of 10% KOH to vaginal secretions.
- Vaginal PH> 4.5 and
- Presence of clue cells on light microscopy.

Complications: BV remains a risk factor for HIV. It also leads to following more common obstetric and gynaecological complications.

Obstetric complications
Chorioaminonitis
Pre-term labour
Pre-maturity
Post-partum fever

Gynaecologicalcomplications
Post-abortion fever
Post-hystrectomy fever
Cuff infection
Chronic mast cell endometritis.
Cervical inflammation and low grade dysplasia

Trichomoniasis:

Epidemiology: A world-wide distribution of approximately 180 million annual cases is known. The infection is diagnosed in about 5% of women in family planning clinics, 13-25% of women attending Gynaec Clinics, in 50-75% of prostitutes and in 7-35% of women in STD clinics.

Pathogenesis and pathology: Sexual transmission remains the main mode of introduction of causative organism trichomonas vaginalis into the vagina. T. vaginalis was identified in urethra of 70% of men after contact with infected women within previous 48 hours. A high prevalence of gonorrhaea is seen with trichomoniasis and both infections are significantly associated with non barrier method of contraception. Recurrent trichomoniasis is common and indicates lack of significant protective immunity. T. vaginalis destroyes the epithelial cells by direct cell contact and cytotoxicity. The urethra and Skene's glands are infected in the majority of patients and organisms are occasionally isolated from the bladder in urine.

Prevention: Barrier contraception efficiently prevents sexual transmission of trichomonads. Spermicidal agents like non-oxynon-9 also reduces transmissions. Re-infection of women is common and simultaneous treatment of sexual partner becomes mandatory.

Clinical features: Infection with T. vaginalis in women ranges from an asymptomatic carrier state to severe acute inflammatory disease. Vaginal discharge is reported by 50-75% of women with trichomoniasis. However, discharge is not always malodorous, yellow

green, frothy and frequently grayish white. 25-50% patients complain of pruritis which is often severe. Other symptoms include dyspareuria, dysuria and rarely frequency of micturition. Less than 10% patients complain of lower abdominal pain which should draw the attention to concomitant salpingitis caused by other organisms. Symptoms appear during or immediately after menstruation. Vulvar erythema is seen in 10-33% cases. Vaginal walls are erythematous and in severe cases may be granular in appearance. Punctate haemorrhages (Colpitis macularis) of the cervix gives it a strawberry like appearance. In 1-2% cases this is apparent on naked eye examination but on colposcopy can be seen in 45% cases. If untreated it is associated with PROM and prematurity. Trichomoniasis is reported to facilitate HIV transmission.

Vulvovaginal candidiasis (VVC): Candida spp. are now found to be the second commonest cause of vaginal infections. It is estimated that 75% of women experience at least one episode of VVC during their child bearing years and approximately 40-50% experience a second attack. Around 5% adult females suffer from repeated, recurrent and often intractable episodes of candida vaginitis. Candida spp. may be isolated from the genital tract of around 20% of asymptomatic healthy women of child bearing age. Factors associated with increased rates of asymptomatic vaginal colonization with candida spp. are pregnancy, use of oral contraceptives and uncontrolled diabetes mellitus. The hormonal dependence of VVC is understood by rarity of candia spp. isolation in premenarchal girls and post-menopausal women.

Pathogenesis and pathology: About 85-90% of yeast isolated from the vagina are candia albicans strain. The other strains seen are candida glabrata and candida tropicalis. Germination of candida spp. enhances colonization and facilitates tissue invasion. Factors like estrogen therapy and pregnancy enhance germination and tend to precipitate symptomatic vaginitis. Candida organism gains access to the vaginal lumen predominantly from the adjacent perianal area.

Clinical features: The most frequent symptoms of VVC is vulvar pruritis. Vaginal discharge is frequenely minimal, described as typically cottage cheese like in character and may vary from watery to homogeneously thick. Vaginal soreness, irritation, dyspareunia external dysuria and vulvar burning are commonly present. Odor if present is minimal and non offensive.

On examination, erythema and swelling of the labia and vulva is seen with discrete pustulopapular peripheral lesions and linear fissures. The cervix is normal and vaginal mucosal erythema with adherent whitish discharge is present. VVC is readily diagnosed by simple microscopic examination of vaginal secreations. A wet mount or saline preparation has 40-60% sensitivity. 10% KOH preparation is more sensitive in diagnosing the presence of germinated yeast. Vaginal PH remains normal (4.0-4.5) in candida infection whereas PH in excess of 4.5 should suggest possibility of bacterial vaginosis (BV), trichomoniasis or mixed infection.

Cervicitis:

Purulent exudates in the cervical os has been highly associated with cervical infections with Chlamydia, trichomonas, N. gonorrhoea, herpes simplex and cytomegalovirus. Many a times mucopurulent endocervicitis and ectocervicites are seen in absence of these pathogens indicating that additional unrecognized causes exist. Risk factors of cervitis include young age, unmarried status, lower socio-economic status, number and recent change of sexual partner, ectopy, oral contraceptive use and concurrent gonococcal infection.

Clinical features and diagnosis

Cervicitis is frequently asymptomatic and is detected on routine pelvic examination. Cervical inflammation is seen because of signs and symptoms of concomitant infections like vaginal trichomoniasis, genital herpes or salpingitis. Mucopurulent cervicites results in purulent vaginal discharge and endocervicitis results in swelling and erythema of the zone of ectopy associated with friability, contact bleeding, spotting and a yellow or green endocervical exudates. Trichomoniasis is associated with ectocervical squamous epithelial mucosal inflammation giving the cervix a strawberry appearance due to microscopic focal patchy petechia (colpitis macularis) in 5-20% of patients. Women with cervicitis may present with associated fever, chills and uterine tenderness. Women who use an IUCD are prone to infections with actinomycetes. 10-30 polymorphonuclear leukocytes per oil immersion field on gram stain of cervical discharge are essential for diagnosis of cervicitis. Ligase chain reaction (LCR) and polymerase chain reaction (PCR) tests for rapid diagnosis of cervicitis by C. trachomatis and N. gonorrhea are as well essential.

Complications: Cervicitis caused by Chlamydia or gonorrhea infection progresses to PID in 10-40% cases. The other known complications are Fitz-Hugh-curtis syndrome or perihepatitis, post partum endometritis, post abortion infection, premature rupture of membranes, preterm labour and small for gestational age infants. Infection acquired by infant during delivery leads to pneumonia in 40-50%, nasopharyngeal infection and opthalmia neonatorum.

Prognosis and prevention

10-40% of cervicitis cases caused by gonococcal and chiamydial infection can progress to PID and inturn infertility. All sexual partners of the patients should be promptly treated. Effects of untreated cervicitis in pregnant women and neonates can be minimized by screening and prompt treatment of high risk pregnant women when seen antenatally. Erythromycin ointment or silver nitrate eye drops are helpful in prophylaxis against opthalmia neonateorum.

Conclusion

Lower reproductive tract infections are

common in sexually active and also in unmarried girls. Clinical features are overlapping. However, do give a clue to the underlying organism. Diagnosis is easily established by routine microscopic techniques and complimented by newer modalities like ELISA, PCR etc. Complications range from mild pruritis and dyspareunia to frank infertility. Treatment needs to be immediate, thorough and directed towards both partners. Results of appropriate therapy are generally gratifying.

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COMMENT

IS THERE A ROLE OF SCREENING FOR COLORECTAL CANCERS?

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Colorectal cancers are the third most common cancer in both men and women, ranking below prostate and lung cancers in men and below breast and lung cancers in women. Cancers of the colon and rectum were predicted to number 148,300 (11.5% of the total patients having malignancies).. The incidence of colon cancer rises with increasing age [1]. 555,000 people were expected to die of cancer every year and about 10% of them die because of cancers of the colon or rectum.[1] Only lung cancer causes more cancer-related deaths.

By definition, the term ***screening*** generally refers to the testing of asymptomatic persons in a large population. Any method by which the disease is detected in a normal person is termed as screening. It involves the testing of a large population to identify persons who are likely to have a specific disease, preferably before it has reached the point where it is manifested clinically. The value of a screening test depends on many factors, including benefits, costs, evidence of its effectiveness, and patient preference and the complications encountered. Many different screening tests are available for colorectal cancer screening, and each meets these criteria to different degrees.[2,3]

Several guidelines are available to assist the attending physicians in deciding how to screen for colorectal cancer. The population to be screened includes persons aged 50 to 80. The risk of colorectal cancer in persons younger than 50 years is too low to justify widespread testing, a conclusion supported by a recent retrospective evaluation of patients in Indianapolis[4]. Although there is less evidence about when to stop screening, it is generally accepted that the potential survival benefit of early detection of adenomatous polyps in persons older than 80 years is small because of an increased likelihood of death from concurrent illness.

These age guidelines apply only to patients who do not have other factors that increase their risk of colorectal cancer. Patients with certain health criteria are known to be at higher risk than the general population and should be tested at an earlier age. Those with a personal history of adenomatous polyps or colorectal cancer require more aggressive surveillance. Patients with an immediate family history of these conditions are more likely to have colonic neoplasms, especially if their relatives are known to have genetic syndromes (e.g., familial adenomatous polyposis, hereditary nonpolyposis colorectal cancer,).

Patients with such symptoms as rectal bleeding or those with other gastrointestinal disorders, such as inflammatory bowel disease (Ulcerative Colitis), may be at increased risk; testing should be chosen on the basis of individual history. In general, colonoscopy is considered the examination of choice for persons believed to be at increased risk of colorectal cancer.

For most patients who are at average risk, there are a number of acceptable alternatives. After appropriate discussion of the benefits, risks, and costs of each approach, the attending clinician and patient can choose from these options:

(1) a fecal occult blood test annually
(2) a rigid sigmoidoscopy/ 60-cm flexible every 5 years,
(3) a combination of a fecal occult blood test annually and a 60-cm flexible/rigid sigmoidoscopy every 5 years
(4) total colon evaluation using colonoscopy, flexible

sigmoidoscopy with fluoroscopic barium, or double-contrast barium enema every 5 years. The I.C.S.I(Institute of Clinical Studies Improvement)guidelines suggest a screening colonoscopy every 5 to 10 years, but several other references, including the revised US Preventive Services Task Force guidelines , state that 10 years is most appropriate[4].

If the examination is felt to be inadequate for any reason (e.g., poor visualization), it should be done a second time or a different test should be performed. Positive findings include the presence of blood identified by fecal occult blood test or the visualization of an invasive cancer, polyp, and source of bleeding, or mucosal abnormality. Diverticula's and hyperplastic polyps are not believed to be precursors to cancer.

The goal of colorectal cancer screening is to identify cancers and polyps or mucosal masses in the colon and rectum. Hyperplastic polyps are the most common nonneoplastic polyps, comprising 10% to 30% of all polyps. They are small in size usually (<0.5 cm in diameter), occur mostly in the distal sigmoid and rectum, and are of no clinical importance. Other benign polyps include mucosal tags and lipomas. When a polyp 5 mm in diameter or smaller is seen during flexible sigmoidoscopy, an attempt should be made to obtain a biopsy specimen. If this effort is unsuccessful or if pathologic assessment confirms that the polyp is adenomatous, the patient should be referred for colonoscopy at the earliest. Because the size of a lesion correlates positively with the risk of cancer, patients with a polyp larger than 10 mm also should be sent for colonoscopic visualization of the entire large bowel and excision of the lesion. Patients with a polyp of intermediate size should be referred for colonoscopy or have a biopsy specimen obtained. If a polyp is found to be hyperplastic on biopsy, no further treatment is needed. Abnormal results of a fecal occult blood test or suspicious findings on double-contrast barium enema also should lead to colonoscopy.

Of all polyps found during colonoscopy, 50% to 70% are adenomatous polyps (adenomas), which are generally premalignant or neoplastic. Only about one third of adenomas are proximal to the splenic flexure; this proportion increases with age. It is generally accepted that more than 95% of colorectal cancers arise in benign adenomatous polyps that develop in the large bowel over several years. This malignant transformation is often called the adenoma-carcinoma sequence, a term that was first used in 1951. Most adenomas remain benign. Each year, only 2.5 polyps per 1,000 turn malignant. The malignant transformation occurs slowly over an average of 10 years, and the risk of malignant transformation correlates with a polyp's size. Polyps larger than 1 cm are more likely to contain high-grade dysplasia or cancer and to be accompanied by other adenomas or cancer elsewhere in the colon[6,7]

"Methods of screening in colorectal cancers"

There are different methods by which screening is done and each has its own merits and demerits as discussed below.

1.FECAL OCCULT BLOOD TEST

The detection of blood in stools is one of the simplest and non-invasive screening tests employed for colorectal cancers. Total Gastrointestinal blood loss in normal individuals is 0.5±0.4 ml/day. There is no defined level which separates basal from pathological blood loss but usually the test will detect losses of more than 10ml/day.Because cancer and polyps bleed more than normal colonic mucosa, the fecal occult blood test often is used as a screening tool. This test depends on the oxidative conversion of a colorless compound to a colored one (blue) in the presence of the pseudoperoxidase activity of hemoglobin.

Patients submit six fecal smears on guaiac-impregnated paper from three consecutive stools. In a developing country like India the sample collected is directly brought to the laboratory, as dipstick method is not used frequently. The detection of blood means that the likelihood of colorectal cancer is higher than normal and requires further investigation, usually by more invasive methods like colonoscopy. Five prospective controlled studies involving 320,000 persons have shown that the fecal occult blood test leads to a 15% to 43% reduction in the mortality rate. However, it has low sensitivity for detecting precancerous polyps, especially small ones.[3,4,7] False-positive test results can occur when foods containing hemoglobin are consumed or when there is gastrointestinal bleeding from another source (e.g., hemorrhoids, gastropathy caused by use of nonsteroidal anti-inflammatory drugs). False-negative test results are most likely to happen if the test is performed when the polyp or neoplasm is not bleeding, but they can also be caused by the interference of antioxidants (e.g., ascorbic acid) with test reagents. The chemicals in toilet cleaners also can damage the reagents. Recommendations to decrease the frequency of inaccurate results are listed below.

1. Collect samples from 3 consecutive bowel movements on different days.
2. Do not collect sample if blood is visible in stool or urine (e.g., from menstruation, hemorrhoids) or patient has bleeding from gums or has used dental floss.
3. Collect sample before contact with toilet water.
4. Return sample to laboratory as quickly as possible.
5. Protect sample from heat, light, and volatile chemicals (e.g., toilet cleaners).

Drugs

6. Avoid nonsteroidal anti-inflammatory drugs for 7 days and vit C supplements before and during stool collection period.
7. Acetaminophen can be taken if required.

Diet

8. Avoid red meats, horseradish, spinach, cauliflower, bananas and citrus fruits and juices for 3

days before and during stool collection period.

9. Eat a well-balanced diet that includes fiber, such as bran cereals, fruits, and vegetables.

The advantages of the test are that it is Inexpensive, has High patient acceptance, has shown to reduce mortality and can detect lesions in even in proximal colon. The disadvantages are that False-positive results may lead to unnecessary colonoscopy, it is Insensitive to precancerous polyps, it has significant false-negative result rate and is Unable to distinguish colonic bleeding from source elsewhere in gastrointestinal tract like angiodysplasia or diverticular diseases.

2.FLEXIBLE/RIGID SIGMOIDOSCOPY

This examination allows direct visualization of the distal colon and provides an opportunity to obtain biopsy specimens of suspicious lesions. With appropriate training, primary care physicians can safely and effectively use the 60-cm sigmoidoscope in their clinics, resulting in greater convenience and acceptance by patients. The techniques involved are well described by Johnson[8]. In Kashmir we are still using the rigid sigmoidoscope in most of our centers. Patient preparation most often involves the use of one or two sodium phosphate enemas (often self-administered prior to the hospital visit), but one study[9] suggested that use of an oral sodium phosphate preparation resulted in a superior-quality endoscopic examination. Allowing the patient only liquids one day prior to the examination helps in having a clean distal bowel.

Up to 60% of colon cancers in the distal bowel are identified using this technique. Nearly all cancers and polyps larger than 1 cm in diameter and smaller polyps can be seen. Cohort and case-controlled studies have shown that screening sigmoidoscopy can reduce deaths from distal cancers by 60% to 85%. When adenomatous polyps or cancers are found, further diagnostic evaluation of the entire colon is indicated.[6,7,10]

It is sometimes recommended that the fecal occult blood test and sigmoidoscopy be combined in a screening program because they seem to complement one another. The fecal occult blood test can detect some lesions in the proximal colon that are beyond the reach of the sigmoidoscope, and the latter can find many polyps or nonbleeding cancers that are missed by the former.[6]

The advantages of sigmoidoscopy are Moderate cost, can often be performed by patient's primary care physician, Shown to reduce disease and death from distal cancers, Preparation is well-tolerated and Specimens of lesion can be obtained for biopsy. The disadvantages are Unable to detect lesions proximal to splenic flexure (about 40% of colon cancers, Not as well suited as colonoscopy for removal of polyps (especially larger ones). Bowel perforation is a potentially serious but rare complication which can be minimized by advancing the cope under vision especially at the sites of bends in the rectum and sigmoid. Cramping and bloating are common effects reported by the patient, which cause some discomfort.

3.DOUBLE-CONTRAST BARIUM ENEMA

The double-contrast barium enema is favored for detection of small mucosal lesions. In this procedure, which is also called an air-contrast barium enema, air is inserted after most of the barium has been removed from the gut. A thin layer of barium sticking to the distended colonic walls delineates and even small lesions can be detected. For evaluation of colonic obstruction thin single-contrast barium study is better. Sensitivity of this method depends on the size of the lesion. 50% to 80% of polyps less than 1 cm in diameter and 70% to 90% of polyps 1 cm or larger can be visualized.

Although no studies have evaluated whether screening by barium enema alone reduces death from colorectal cancer, the ability of the barium enema to find polyps has led to its inclusion as a screening option in guidelines addressing this topic. It is recommended for use every 5 years in an asymptomatic population. As with the fecal occult blood test and sigmoidoscopy, further diagnostic evaluation of the colon by other means is necessary if abnormalities are found [10,11]. The major disadvantage is that you cannot take the biopsy of a lesion if and when detected for which the patient needs more invasive procedures.

4.COLONOSCOPY

A full colonic assessment is best accomplished by colonoscopy, which was introduced in the early 1970s. The degree of visualisation varies with the experience of the endoscopist and the adequacy of bowel preparation. The cecum can be reached in up to 98% of examinations and the whole large colon can be visualised. Patients who are not taking diuretics and do not have renal, cardiovascular, or electrolyte disorders can safely prepare for the test by ingesting an oral sodium phosphate solution the day before and the day of the test. Patients with risk factors for these disorders should use a safer, albeit less palatable, oral lavage preparation, such as Polyethylene glycol.

Although no studies have shown that screening with colonoscopy reduces the number of deaths from cancer, it is often considered the "gold standard" among tests that look for lesions within the colon. An investigation conducted at 13 Veterans Affairs medical centers and involving more than 3,000 patients confirmed that colonoscopic screening could be a useful tool to detect neoplasms in asymptomatic adults.[12]

One of the most cited articles supporting the efficacy of colonoscopy and polypectomy in reducing colorectal cancer is the 1993 report of the National Polyp Study [13]. In the study, excision of adenomas reduced the incidence of cancer by 76% to 90% compared with three different reference groups.

It has been suggested that colonoscopy is the screening test of choice. However, there are several barriers to the widespread use of colonoscopy for screening in the general population: it usually requires sedation, has higher risks (e.g., perforation of the bowel,

reaction to sedatives) than other screening techniques, must be performed in an endoscopy room, and is more expensive than the other tests discussed in this article. In our valley the patients have to wait for a longer period of time than is desirable as it is available at only some centers.. The patients also dislike the bowel preparation required for the test.

The future of screening for colorectal cancers

Although the value of screening for colorectal cancer is generally accepted, a number of questions remain. There is increasing support in the literature for use of colonoscopy as the screening examination of choice, even with the associated increase in cost and potential complications [14]. Funding issues need to be addressed, because adoption of this procedure for screening is limited by the incurrence of cost in its use in an asymptomatic population[15,16]

Finally, other screening methods, such as computed tomographic colography (virtual colonoscopy)[17] and testing of stool specimens for genetic markers, are being developed with the hope that they will make regular testing for colorectal cancer agreeable, or even attractive to most patients. The advances in molecular biology have led to the definitions of many of the genetic mutations associated in the progression from normal colonic mucosa to malignancy[18,19] and has raised the possibility of genetic screening[20]. Although there has been an improvement in the overall survival in patients having colorectal carcinomas in the last 3 decades[21] prognosis is still related to the extent of spread at the time of diagnosis.[22] Albumin has also been suggested as an alternative feacal marker as it is easily lost into the gut in case of tissue or capillary damage [10,23]. Recently plasma protein a_1 antitrypsin is being investigated as a possible marker.[10] for screening. The tumour specific antigen Carcinoembryonic antigen is also having both a screening role as well as a prognostic role.[10,23] Whatever approach is taken, it seems clear that screening for colorectal cancer has a definite role to play and can reduces disease and saves lives.

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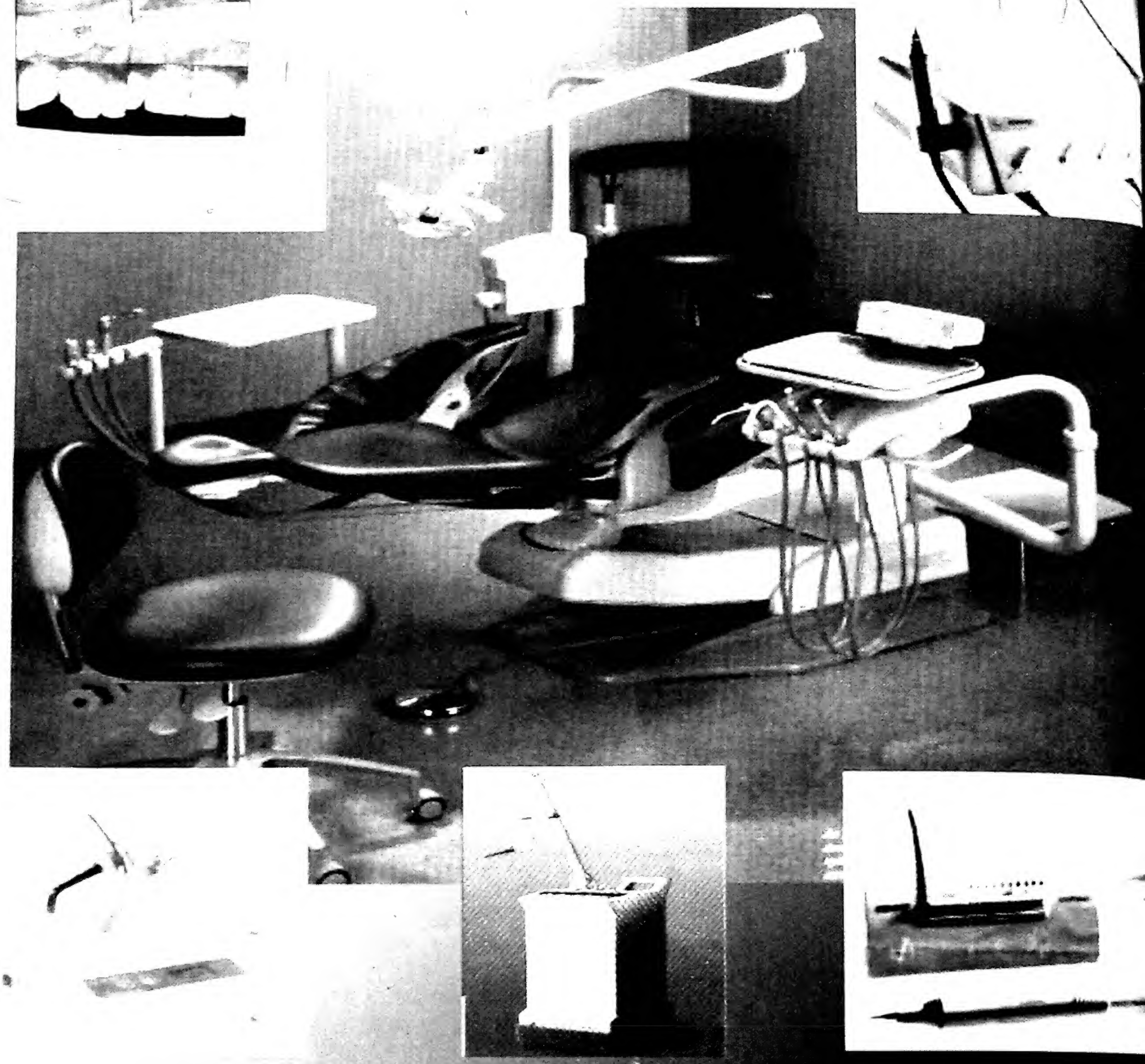

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Avian influenza- Recent concepts & current situation

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Influenza Viruses

Influenza viruses are pleomorphic, enveloped, with segmented negative-strand RNA genomes, and belong to the family orthomyxoviridae (Fig 1). There are three types of influenza viruses: A, B, and C[1]. Influenza type A viruses can infect people, birds, pigs, horses, seals, whales and other animals. Wild birds are the natural hosts for these viruses(Fig 2). Influenza type A viruses are divided into subtypes based on two proteins on the surface of the virus. These proteins are called hemagglutinin (HA) and neuraminidase (NA). There are 15 different HA subtypes and 9 different NA subtypes. Many different combinations of HA and NA proteins are possible. Subtypes of influenza A virus are named according to their HA and NA surface proteins. For example, an "H7N2 virus" designates an influenza A subtype that has an HA 7 protein and an NA 2 protein. Similarly an "H5N1" virus has an HA 5 protein and an NA 1 protein. Only some influenza A subtypes (i.e., H1N1, H1N2, and H3N2) are currently in general circulation among people. Other subtypes are found most commonly in other animal species. For example, H7N7 and H3N8 viruses cause illness in horses. Influenza B viruses are normally found only in humans. Unlike influenza A viruses, these viruses are not classified according to subtype. Although influenza type B viruses can cause human epidemics, they have not caused pandemics. Influenza type C viruses cause mild illness in humans and do not cause epidemics or pandemics. These viruses are not classified according to subtype.

Influenza B viruses and subtypes of influenza A virus are further characterized into strains. There are many different strains of influenza B viruses and of influenza A subtypes. New strains of influenza viruses appear and replace older strains. Influenza viruses can change in two different ways. One type is called "antigenic drift," which occurs through small changes in the virus that happen continually over time. Antigenic drift produces new virus strains that may not be recognized by antibodies to earlier influenza strains. This process works as follows: a person infected with a particular flu virus strain develops antibody against that virus. As newer virus strains appear, the antibodies against the older strains no longer recognize the "newer" virus, and infection with a new strain can occur. This is one of the main reasons why people can get the flu more than one time. In most years, one or two of the three virus strains in the influenza vaccine are updated to keep up with the changes in the circulating flu viruses. For this reason, people who want to be immunized against influenza need to receive a flu vaccination every year. The other type of change is called "antigenic shift." Antigenic shift is an abrupt, major change in the influenza A viruses, resulting in a new influenza virus that can infect humans and has a hemagglutinin protein or hemagglutinin and neuraminidase protein combination that has not been seen in humans for many years. Antigenic shift results in a new influenza A subtype. If a new subtype of influenza A virus is introduced into the human population, most people have little or no protection against the new virus, and if the virus can spread easily from person to person, a pandemic (worldwide spread) may occur. Influenza viruses are changing by antigenic drift all the time, but antigenic shift happens only occasionally. Influenza type A viruses undergo both kinds of changes; influenza type B viruses change only by the more gradual process of antigenic drift.

Humans can be infected with influenza types A, B, and C. However, the only subtypes of influenza A virus that normally infect people are influenza A subtypes H1N1, H1N2, and H3N2. Between 1957 and 1968, H2N2 viruses also circulated among people, but currently do not. Only influenza A viruses infect birds. Wild birds are the natural host for all subtypes of influenza A virus. Typically wild birds do not get sick when they are infected with influenza virus. However, domestic poultry, such as turkeys and chickens, can get very sick and die from avian influenza, and some avian viruses also can cause serious disease and death in wild birds.

H5 and H7 subtypes of avian influenza A viruses can be further classified as either highly pathogenic avian influenza (HPAI) or low pathogenic avian influenza (LPAI). This distinction is made on the basis of genetic features of the virus. HPAI is usually associated with high mortality in poultry. HPAI viruses can kill 90 to 100% of infected chickens, whereas LPAI viruses cause less severe or no illness if they infect chickens. Because LPAI viruses can evolve into HPAI viruses, outbreaks of H5 and H7 LPAI are closely monitored by animal health officials.

Influenza pandemics

An influenza pandemic is a global outbreak of disease that occurs when a new influenza A virus appears or "emerges" in the human population, causes serious illness, and then spreads easily from person to person worldwide[2]. Pandemics are different from seasonal outbreaks or "epidemics" of influenza. Seasonal outbreaks are caused by subtypes of influenza viruses that already

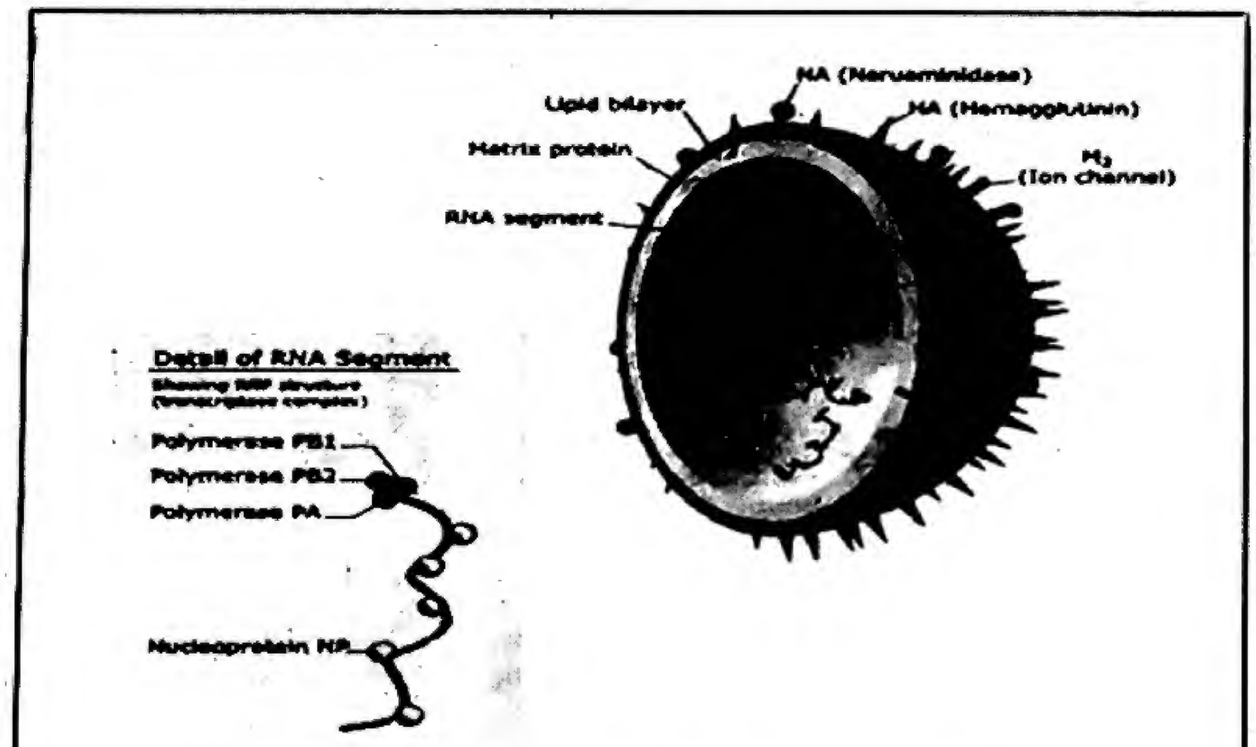

Figure 1. Showing Structure of Influenza Virus

circulate among people, whereas pandemic outbreaks are caused by new subtypes, by subtypes that have never circulated among people, or by subtypes that have not circulated among people for a long time. Past influenza pandemics have led to high levels of illness, death, social disruption, and economic loss. A pandemic can start when three conditions have been met: a new influenza virus subtype emerges; it infects humans, causing serious illness; and it spreads easily and sustainably among humans. The H5N1 virus amply meets the first two conditions: it is a new virus for humans (H5N1 viruses have never circulated widely among people), and it has infected more than 100 humans, killing over half of them. No one will have immunity should an H5N1-like pandemic virus emerge. All prerequisites for the start of a pandemic have therefore been met save one: the establishment of efficient and sustained human-to-human transmission of the virus. The risk that the H5N1 virus will acquire this ability will persist as long as opportunities for human infections occur. These opportunities, in turn, will persist as long as the virus continues to

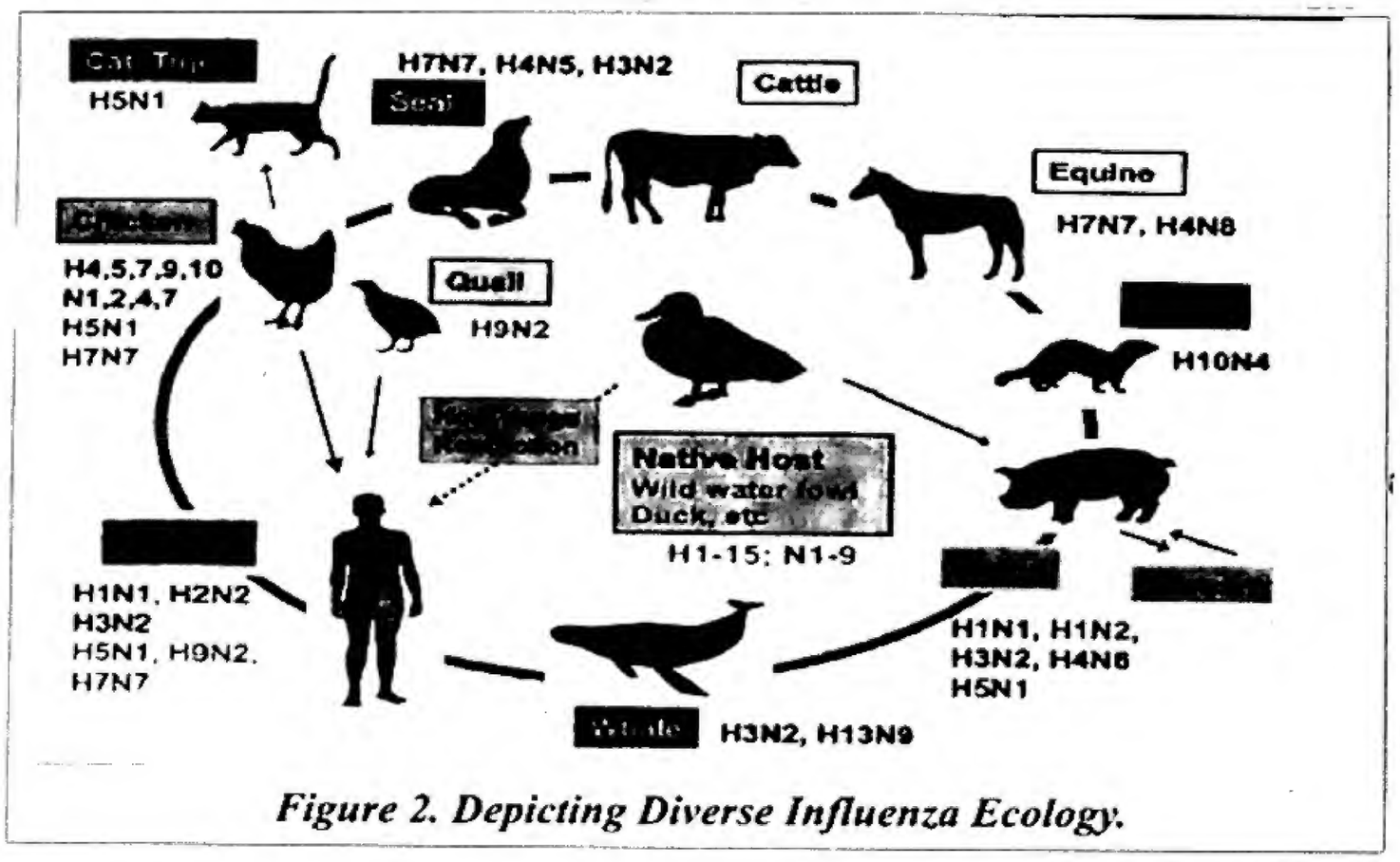

Figure 2. Depicting Diverse Influenza Ecology.

circulate in birds, and this situation could endure for some years to come.

Pandemic viruses emerge as a result of a process called "antigenic shift," which causes an abrupt or sudden, major change in influenza A viruses. These changes are caused by new combinations of the HA and/or NA proteins on the surface of the virus. Changes results in a new influenza A virus subtype. The appearance of a new influenza A virus subtype is the first step toward a pandemic; however, to cause a pandemic, the new virus subtype also must have the capacity to spread easily from person to person. Once a new pandemic influenza virus emerges and spreads, it usually becomes established among people and moves around or "circulates" for many years as seasonal epidemics of influenza. The U.S. Centers for Disease Control and Prevention (CDC) and the World Health Organization (WHO) have large surveillance programs to monitor and detect influenza activity around the world, including the emergence of possible pandemic strains of influenza virus.

The risk of pandemic influenza is serious. With the H5N1 virus now firmly entrenched in large parts of Asia, the risk that more human cases will occur will persist. Each additional human case gives the virus an opportunity to improve its transmissibility in humans, and thus develop into a pandemic strain. The recent spread of the virus to poultry and wild birds in new areas further broadens opportunities for human cases to occur. While neither the timing nor the severity of the next pandemic can be predicted, the probability that a pandemic will occur has increased. There are several other causes for concern

- Domestic ducks can now excrete large quantities of highly pathogenic virus without showing signs of illness, and are now acting as a "silent" reservoir of the virus, perpetuating transmission to other birds. This adds yet another layer of complexity to control efforts and removes the warning signal for humans to avoid risky behaviors.
- When compared with H5N1 viruses from 1997 and early 2004, H5N1 viruses now circulating are more lethal to experimentally infected mice and to ferrets and survive longer in the environment.
- H5N1 appears to have expanded its host range, infecting and killing mammalian species previously considered resistant to infection with avian influenza viruses.
- The behavior of the virus in its natural reservoir, wild waterfowl, may be changing. The spring 2005 die-off of upwards of 6,000 migratory birds at a nature reserve in central China, caused by highly pathogenic H5N1, was highly unusual and probably unprecedented. In the past, only two large die-offs in migratory birds, caused by highly pathogenic viruses, are known to have occurred: in South Africa in 1961 (H5N3) and in Hong Kong in the winter of 2002–2003 (H5N1).

During the 20th century, the emergence of several new influenza A virus subtypes caused three pandemics, all of which spread around the world within a year of being detected.

- **1918-19, "Spanish flu,"** [A (H1N1)], caused the highest number of known influenza deaths. (However, the actual influenza virus subtype was not detected in the 1918-19 pandemic). More than 500,000 people died in the United States, and up to 50 million people may have died worldwide. Many people died within the first few days after infection, and others died of secondary complications. Nearly half of those who died were young, healthy adults. Influenza A (H1N1) viruses still circulate today after being introduced again into the human population in 1977.
- **1957-58, "Asian flu,"** [A (H2N2)], caused about 70,000 deaths in the United States. First identified in China in late February 1957, the Asian flu spread to the United States by June 1957.

contaminated with virus. People, vehicles, and other inanimate objects such as cages can be vectors for the spread of influenza virus from one farm to another. When this happens, avian influenza outbreaks can occur among poultry[4]. Avian influenza outbreaks among poultry occur worldwide from time to time. Since 1997, for example, more than 16 outbreaks of H5 and H7 influenza have occurred among poultry in the United States. The U.S. Department of Agriculture monitors these outbreaks. Low pathogenic forms of avian influenza viruses are responsible for most avian influenza outbreaks in poultry. Such outbreaks usually result in either no illness or mild illness (e.g., ruffled feathers, chickens producing fewer or no eggs), or low levels of mortality. When highly pathogenic influenza H5 or H7 viruses cause outbreaks, between 90% and 100% of poultry can die from infection. Animal health officials carefully monitor avian influenza outbreaks in domestic birds for several reasons:

- the potential for low pathogenic H5 and H7 viruses to evolve into highly pathogenic forms
- the potential for rapid spread and significant illness and death among poultry during outbreaks of highly pathogenic avian influenza
- the economic impact and trade restrictions from a highly pathogenic avian influenza outbreak.
- the possibility that avian influenza could be transmitted to humans

When avian influenza outbreaks occur in poultry, quarantine and depopulation (or culling) and surveillance around affected flocks is the preferred control and eradication option.

Is it safe to eat poultry and poultry products?

The answer is yes, though certain precautions should be followed in countries currently experiencing outbreaks. In areas free of the disease, poultry and poultry products can be prepared and consumed as usual (following good hygienic practices and proper cooking), with no fear of acquiring infection with the H5N1 virus. In areas experiencing outbreaks, poultry and poultry products can also be safely consumed provided these items are properly cooked and properly handled during food preparation. The H5N1 virus is sensitive to heat. Normal temperatures used for cooking (70°C in all parts of the food) will kill the virus. Consumers need to be sure that all parts of the poultry are fully cooked (no "pink" parts) and that eggs, too, are properly cooked (no "runny" yolks). In areas experiencing outbreaks in poultry, raw eggs should not be used in foods that will not be further heat-treated as, for example by cooking or baking. Avian influenza is not transmitted through cooked food. To date, no evidence indicates that anyone has become infected following the consumption of properly cooked poultry or poultry products, even when these foods were contaminated with the H5N1 virus.

Avian Influenza Infection in Humans

Although avian influenza A viruses usually do not infect humans, more than 100 confirmed cases of human infection with avian influenza viruses have been reported since 1997[5]. For example, the World Health Organization (WHO) maintains situation updates and cumulative reports of human cases of avian influenza A (H5N1). Most cases of avian influenza infection in humans are thought to have resulted from direct contact with infected poultry or contaminated surfaces. However, there is still a lot to learn about how different subtypes and strains of avian influenza virus might affect humans. For example, it is not known how the distinction between low pathogenic and highly pathogenic strains might impact the health risk to humans. Because of concerns about the potential for more widespread infection in the human population, public health authorities closely monitor outbreaks of human illness associated with avian influenza. To date, human infections with avian influenza A viruses detected since 1997 have not resulted in sustained human-to-human transmission. However, because influenza A viruses have the potential to change and gain the ability to spread easily between people, monitoring for human infection and person-to-person transmission is important. Theoretically, influenza A viruses with a hemagglutinin against which humans have little or no immunity that have reassorted with a human influenza virus are more likely to result in sustained human-to-human transmission and pandemic influenza. Therefore, careful evaluation of influenza viruses recovered from humans who are infected with avian influenza is very important to identify reassortment if it occurs. Confirmed instances of avian influenza viruses infecting humans since 1997 include:

- H5N1, Hong Kong, Special Administrative Region, 1997: Highly pathogenic avian influenza A (H5N1) infections occurred in both poultry and humans. This was the first time an avian influenza A virus transmission directly from birds to humans had been found. During this outbreak, 18 people were hospitalized and six of them died. To control the outbreak, authorities killed about 1.5 million chickens to remove the source of the virus. Scientists determined that the virus spread primarily from birds to humans, though rare person-to-person infection was noted.
- H9N2, China and Hong Kong, Special Administrative Region, 1999: Low pathogenic avian influenza A (H9N2) virus infection was confirmed in two children and resulted in uncomplicated influenza-like illness. Both patients recovered, and no additional cases were confirmed. The source is unknown, but the evidence suggested that poultry was the source of infection and the main mode of transmission was from bird to human. However, the possibility of person-to-person transmission could not be ruled out. Several additional human H9N2 infections were reported from China in 1998-99.
- H7N2, Virginia, 2002: Following an outbreak of H7N2 among poultry in the Shenandoah Valley poultry production area, one person was found to have serologic evidence of infection with H7N2.
- H5N1, China and Hong Kong, Special Administrative Region, 2003: Two cases of highly pathogenic avian influenza A (H5N1) infection occurred among members of a Hong Kong family that had traveled to China. One person recovered, the other died. How or where these two family members were infected was not determined. Another family member died of a respiratory illness in China, but no testing was done.
- H7N7, Netherlands, 2003: The Netherlands reported outbreaks of influenza A (H7N7) in poultry on several farms. Later, infections were reported among pigs and humans. In total, 89 people were confirmed to have H7N7 influenza virus infection associated with this poultry outbreak. These cases occurred mostly among poultry workers. H7N7-associated illness included 78 cases of conjunctivitis (eye infections) only; 5 cases of conjunctivitis and influenza-like illnesses with cough, fever, and muscle aches; 2 cases of influenza-like illness only; and 4 cases that were classified as "other." There was one death among the 89 total cases. It occurred in a veterinarian who visited one of the affected farms and developed acute respiratory distress syndrome and complications related to H7N7 infection. The majority of these cases occurred as a result of direct contact with infected poultry; however, Dutch authorities reported three possible instances of transmission from poultry workers to family members. Since then, no other instances of H7N7 infection among humans have been reported.
- H9N2, Hong Kong, Special Administrative Region, 2003: Low pathogenic avian influenza A (H9N2)

further identification or characterization. Communication and publication of analysis results should be according to the WHO Guidance for the timely sharing of influenza viruses/specimens with potential to cause human influenza pandemics.

2. Inform the WHO Office in the country or WHO Regional Office or WHO HQ Global Influenza Programme that specimens or virus isolates are being forwarded to other Laboratories for further identification or further characterization.

4. **Serological identification of influenza A/H5 infection**

Serological tests available for the measurement of influenza A-specific antibody include the Haemagglutination inhibition test, the enzyme immunoassay, and the virus neutralization tests. The microneutralization assay is the recommended test for the measurement of highly pathogenic avian influenza A specific antibody. Because this test requires the use of live virus, its use for the detection of highly pathogenic avian influenza A specific antibody is restricted to those laboratories with Biosafety Level 3 containment facilities.

Treatment of Avian influenza

Four different antiviral drugs (amantadine, rimantadine, oseltamivir, and zanamivir) are approved by the U.S. Food and Drug Administration (FDA) for the treatment of influenza; First three are approved for prophylaxis also. Early treatment provides the greatest clinical benefit. All four have activity against influenza A viruses. However, sometimes influenza strains can become resistant to these drugs, and therefore the drugs may not always be effective. For example, analyses of some of the 2004 H5N1 viruses isolated from poultry and humans in Asia have shown that the viruses are resistant to two of the medications (amantadine and rimantadine). The H5N1 virus is expected to be susceptible to the neuraminidase inhibitors oseltamivir (commercially known as Tamiflu which is available as pill) and zanamivir (commercially known as Relenza which is available as dry powder). Monitoring of avian influenza A viruses for resistance to influenza antiviral medications is ongoing. For the neuraminidase inhibitors, the main constraints are limited production capacity and a price that is prohibitively high for many countries. At present manufacturing capacity, which has recently quadrupled, it will take a decade to produce enough oseltamivir to treat 20% of the world's population. The manufacturing process for oseltamivir is complex and time-consuming, and is not easily transferred to other facilities.

Avian Influenza Vaccines

Currently no vaccine is available to protect humans against the H5N1 virus that is being seen in Asia. However, vaccine development efforts are under way. Research studies to test a vaccine to protect humans against H5N1 virus began in April 2005 and a series of clinical trials is underway. (Researchers are also working on a vaccine against H9N2, another bird flu virus subtype). Sanofi Pasteur, formerly Aventis Pasteur, was awarded a contract by National Institute of Allergy & infectious diseases (NIAID) to manufacture the H5N1 vaccine in May 2004. This is an inactivated vaccine manufactured from an H5N1 virus isolated in Southeast Asia in 2004. The process of initiation of the trials of this vaccine has begun.

The WHO Influenza Surveillance Network has characterized H5N1 influenza viruses isolated from humans and animals from several countries affected by the 2004/2005 H5N1 outbreak in Asia. WHO has also made recommendations on the antigenic and genetic characteristics of H5N1 viruses which are suitable for vaccine production. In addition, WHO collaborating centres and reference laboratories have developed several recombinant H5N1 prototype vaccine strains[15], including A/Vietnam/1194/04, A/Vietnam/1203/04 and A/Hongkong/213/03, according to the requirements of several major national and international pharmaceutical licensing agencies for influenza vaccine production. These H5N1 influenza pandemic vaccine prototype strains have already been made available to a number of institutions and companies and several different vaccines have been produced for clinical testing. WHO will continue to monitor the antigenic and genetic changes in circulating A/H5N1 viruses, especially in humans. For research purposes, the WHO Collaborating Centres will develop experimental prototype vaccine strains from recent human influenza A/H5N1 viruses.

The timely selection and verification of suitable H5N1 prototype vaccine strains depends primarily on close collaboration between the affected countries and WHO, especially as regards the rapid sharing of A/H5N1 virus/specimens, particularly from humans, and exchange of analytical data. Although a vaccine against the H5N1 virus is under development in several countries, no vaccine is ready for commercial production and no vaccines are expected to be widely available until several months after the start of a pandemic. Because the vaccine needs to closely match the pandemic virus, large-scale commercial production will not start until the new virus has emerged and a pandemic has been declared. Current global production capacity falls far short of the demand expected during a pandemic.

Control measures

Human influenza is thought to transmit primarily via large respiratory droplets. Standard Precautions plus Droplet Precautions are recommended for the care of patients infected with human influenza. All patients who present to a health-care setting with fever and respiratory symptoms should be managed according to recommendations for respiratory hygiene and cough etiquette and questioned regarding their recent travel history. Patients with a history of travel within 10 days to a country with avian influenza activity and are hospitalized with a severe febrile respiratory illness, or are otherwise under evaluation for avian influenza, should be managed using isolation precautions identical to those recommended for patients with known Severe Acute Respiratory Syndrome (SARS)[16]. These include:

Standard Precautions

- Pay careful attention to hand hygiene before and after all patient contact or contact with items potentially contaminated with respiratory secretions.

Contact Precautions

- Use gloves and gown for all patient contact.
- Use dedicated equipment such as stethoscopes, disposable blood pressure cuffs, disposable thermometers, etc.

Eye protection (i.e., goggles or faces shields)

- Wear when within 3 feet of the patient.

Airborne Precautions

- Place the patient in an airborne isolation room (AIR). Such rooms should have monitored negative air pressure in relation to corridor, with 6 to 12 air changes per hour (ACH), and exhaust air directly outside or have recirculated air filtered by a high efficiency particulate air (HEPA) filter. If an AIR is unavailable, contact the health-care facility engineer to assist or use portable HEPA filters to augment the number of ACH.

Use a fit-tested respirator, at least as protective as a National Institute of Occupational Safety and Health (NIOSH)-approved N-95 filtering face piece (i.e., disposable) respirator, when entering the room. These precautions should be continued for 14 days after onset of symptoms or until either an alternative diagnosis is established or diagnostic test results indicate that the patient is not infected with influenza A virus. Patients managed as outpatients or hospitalized patients discharged before 14 days with suspected avian influenza should be isolated in the

home setting on the basis of principles outlined for the home isolation of SARS patients. Health-care workers involved in the care of patients with documented or suspected avian influenza should be vaccinated with the most recent seasonal human influenza vaccine.

Conclusions

Infected birds have been the primary source of influenzaA (H5N1) infections in humans in Asia. Transmission between humans is very limited at present, but continued monitoring is required to identify any increase in viral adaptation to human hosts. Despite an advance warning that has lasted almost two years, the world is ill-prepared to defend itself during a pandemic. WHO has urged all countries to develop preparedness plans, to stockpile antiviral drugs nationally for use at the start of a pandemic. Around 30 countries are purchasing large quantities of these drugs, but the manufacturer has no capacity to fill these orders immediately. On present trends, most developing countries will have no access to vaccines and antiviral drugs throughout the duration of a pandemic. Thus there is an urgent need for more coordination at National as well as International level to effectively face this challenge.

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Association of severity of hepatitis E virus infection in the mother and vertically transmitted infection in the fetus.

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Abstract

Background: Hepatitis E virus infection is vertically transmitted from mother to the fetus, often leading to severe fetal and neonatal disease. The relationship between severity of disease in the mother and fetus is not known. We studied clinical and biochemical characteristics of 36 consecutive pregnant women with acute HEV infection. Babies borne to these women were assessed for vertically transmitted HEV infection and the severity of liver disease in the newborn. The severity of disease in the newborn was correlated with the maternal disease. Of the 36 pregnant women with HEV infection, 20 (55.6%) had nonfulminant disease and 16 (44.4%) had fulminant hepatic failure (FHF). Nine (56.3%) of the 16 mothers with FHF had disseminated intravascular coagulation. Six (37.5%) women with FHF survived and 10 (62.5%) died. Twenty-five (69.4%) infants had HEV infection at birth. Fourteen (56%) of such infants died with a clinical syndrome resembling FHF. Babies borne to mothers with FHF were more often HEV infected and viremic ((15/16; 93.8%% for both) than those with nonfulminant disease (10/20; 50% and 5/20; 25%) (p=0.004 and <0.001 respectively). Twelve (75%) of the 16 babies borne to mothers with FHF had clinical syndrome of FHF because of massive hepatic necrosis. In contrast only two (10%) of the 20 mothers with nonfulminant disease delivered babies who developed FHF (p=0.008) All the six mothers who survived had delivered babies within 4 days (2.3±1.0 days) of onset of encephalopathy. In contrast, all the 10 mothers who died had delivered babies 4 days (9.6±3.0 days) after onset of encephalopathy (p=0.02). The severity of hepatitis E virus infection in the mother and the fetus is related to each other and needs further studies to define cause and affect relationship.

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Hepatitis E virus (HEV) causes large scale water borne epidemic of acute hepatitis in developing countries.[1,2] HEV is the commonest cause of acute sporadic viral hepatitis and fulminant hepatic failure in endemic areas.[3] HEV infections have been reported as imported disease in travelers and tourists from the developed countries to endemic areas.[4] Recently HEV infections have been documented to occur in persons from developed countries, who have never traveled to endemic areas.[5] Such infections may have zoon tic origin.[6]

HEV has unique epidemiologic features. The disease has high attack rate among adults 15-40 years of age. The overall mortality associated with HEV infection is similar to hepatitis A.[1] HEV infection has increased severity among pregnant women.[7] Pregnant women especially in the second and third trimester develop fulminant hepatic failure (FHF). Disseminated intravascular coagulation is a dominant feature during FHF in such women[8] The mortality in the second trimester is around 20% and reaches up to 45% in the third trimester. The clinical course of non-E acute hepatitis in pregnant women is similar to that in non-pregnant women and men[1,8,9] The cause of increased severity of HEV in pregnancy is not known.

HEV is commonly transmitted from infected mother to the fetus and causes serious fetal and neonatal infections with significant fetal loss and perinatal morbidity and mortality.[10,11] Could fetal HEV infection and fetal disease influence the course of maternal HEV infection? In this study, we addressed this issue by correlating the severity of fetal HEV infection with the clinical course of maternal disease in a large cohort of pregnant women with acute HEV infection.

Material and Methods

The study included all consecutive pregnant women with acute HEV infection attending Gastroenterology Department at Sher-I-Kashmir Institute of Medical Sciences Srinagar Kashmir (India) from January 1995 to January 1997. Urinary test for chorionic gonadotrophin and pelvic ultrasound examination were done to detect pregnancy and to evaluate age of gestation. All patients were monitored closely for maternal disease course, complications and outcome. Patients with FHF were admitted to intensive care unit and received standard supportive care with monitoring of clinical, biochemical and hemodynamic parameters. None of the patients received a liver transplant or artificial liver support. Fetal status was reviewed on a daily basis. A conservative and expectant approach was followed and no attempts were made to terminate pregnancy or induce labor unless otherwise indicated on standard obstetric practices (fetal distress etc.). Baby was observed at birth and during the next 2 weeks for any clinical signs of liver disease. Blood samples from mothers and babies (at birth and at 2 weeks) were collected for biochemical and serological tests. A serum sample was stored at –70·C for subsequent virological assays.

The criteria for the diagnosis of icteric AVH were[1] recent onset of jaundice

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in the absence of prior history of jaundice or chronic liver disease;[2] no other cause to account for jaundice, including drug hepatitis, severe infections, cholestatic jaundice of pregnancy, eclampsia, HELLP syndrome, acute fatty liver of pregnancy etc (if any of the above diagnoses was entertained, appropriate clinical examination, imaging tools and laboratory tests were utilized to substantiate the diagnosis); [3]serum bilirubin of 2.0 mg/dl or more, with an increase in transaminases two and a half times above the upper limit of normal {serum aspartate aminotransferase (AST) 6 to 18 IU/liter; serum alanine aminotransferase (ALT) 3 to 26 IU/liter}); [4]liver biopsy in selected group of patients substantiating diagnosis of acute viral hepatitis. Postmortem liver biopsies were performed in all fatal cases (mothers and babies). Anicteric AVH was defined if all the above criteria were fulfilled except elevated serum bilirubin (serum bilirubin d"2mg/dl) [1,3,8]

FHF was defined as the occurrence of hepatic encephalopathy in a patient with AVH within eight weeks of onset of the disease. Encephalopathy was classified into four grades as per defined criteria. Cerebral edema in such patients was diagnosed when features of decerebration occurred, along with other clinical signs of high intracranial pressure. Disseminated intravascular coagulation (DIC) was diagnosed when bleeding occurred from multiple anatomical sites (skin, mucosa, venipuncture sites etc.) along with low levels of fibrinogen (<2g/l), thrombocytopenia (<100x10⁹/l), and high levels of fibrin degradation products [3]

Vertical HEV infection (from mother-to-fetus) in a pregnant woman with acute HEV infection was diagnosed when the blood collected from the baby at birth or within 2 weeks of birth (minimum incubation period of the disease) had IgM anti-HEV or HEV RNA [9] A baby was defined to have FHF once following criteria were fulfilled 1. baby borne with or developed icteric AVH in the first 2 weeks of birth; 2. clinical state of unresponsiveness, hypoglycemia, hypothermia and convulsions; 3. postmortem needle biopsies of liver showing evidence of massive hepatic necrosis. Such a clinical course has been recognized by others and us in the infants dying of FHF caused by vertically transmitted HEV infection.[10,11]

Serology for hepatitis viruses was performed by enzyme immunosorbant assays (ELISA) for markers of HAV (IgM anti-HAV), HBV (HBsAg and IgM anti-HBc), HCV (anti-HCV 2-generation) and HDV (IgG and IgM anti-HDV) using commercially available kits from Abbott Laboratories (North Chicago IL). The assays were performed strictly according to manufacturer's instructions. Sera from all patients were also tested by ELISA for IgG and IgM antibodies to HEV by a kit using two recombinant HEV antigens corresponding to structural region of the HEV (Diagnostic Biotechnology Singapore). All sera were tested by PCR for HEV RNA and HCV RNA. The detection of HEV RNA was performed by reverse transcription nested PCR using primer sets 3043/3044 and HEV-1/HEV-3. The primer sequences and the conditions for PCR have been previously described.[10] HCV RNA was detected by reverse-transcription nested PCR using primer from the 5' non-translated region. To avoid bias, all sera were tested under code. Confirmed positive and negative controls were run with all PCR amplification reactions to ensure faithful amplifications. Strict application of containment measures was used to avoid false positives. Results of any PCR reactions were considered valid only if they were consistent in at least two independent experiments that included RNA extraction step as well.

On the basis of above viral markers, AVH was classified as: HA (presence of IgM anti-HAV), AHB (presence of HBsAg and IgM anti-HBc), acute hepatitis on a HB carrier (presence of HBsAg with negative IgM anti-HBc), HD (presence of IgG or IgM anti-HDV and HBsAg), HCV infection (presence of anti-HCV and/or HCV RNA), HEV (presence of IgM anti-HEV and/or HEV RNA) and HNAE (negative of above viral markers).

Statistical methods Comparisons of categorical variables were analyzed using either Fisher's exact test when any of the expected value was less than 5 or chi-square test for all others. Comparisons of continuous variables were analyzed using student's t-test for normally distributed variables and Mann-Whitney U test for non-normally distributed variables. Variables with skewed deviation (serum bilirubin and ALT) were normalized using log transformation for analysis. All values are expressed as mean ± 1SD. A p value of <0.05 was considered significant.

Results

The study included 36 pregnant women (age, mean±1SD; 26.4±4.8 years). One mother was in first trimester, 6 in second trimester and 19 in third trimester. Sixteen (44.4%) mothers had developed FHF. Of these, 13 presented with clinical features of FHF and another 3 develop FHF during the hospital course. The clinical course of 9 (56.3%) patients with FHF was complicated by DIC. Ten (62.5%) of the 16 mothers with FHF died and 6 (37.5%) survived. Remaining 20 (55.6%) mothers had nonfulminant course of illness with clinical, biochemical and serologic recovery in 4.3±1.2 weeks (range 2 to 8 weeks).

All the 36 women delivered vaginally. This included 3 abortions, 7 premature deliveries and 26 full term deliveries. Twenty-five (69.4%) babies at birth revealed evidence of HEV infection (IgM anti-HEV positive in 24 and HEV RNA reactive in 20). Two (8%) had anicteric hepatitis (elevated ALT with normal serum bilirubin) and 23 (92%) had icteric HEV infection. All infants were negative for evidence of neonatal infections such as toxoplasmosis, rubella virus, cytomegalovirus, and herpes simplex virus (TORCH complex). Fourteen (60.9%) of the 23 babies with icteric hepatitis were borne with a clinical state of unresponsiveness, hypoglycemia and hypothermia and died in the first week of birth. Such a clinical course has been recognized by us and others in the infants dying of FHF caused by vertically transmitted HEV infection [10,11] Postmortem needle biopsies of liver were performed in these babies and revealed evidence of massive hepatic necrosis.

Table 1 compares various parameters between mothers with nonfulminant (n=20) vs. fulminant HEV infection (n=16). Pregnant women with FHF had similar age, trimester distribution, serum bilirubin and ALT when compared to those with nonfulminant disease. However, babies borne to mothers with FHF in comparison to those with nonfulminant hepatitis were more often infected with HEV (93.8% vs. 50%; p=0.004) and higher proportions of such infected babies were viremic (93.8% vs. 25%; p=<0.001). Twelve (75%) of the 16 babies with HEV infections borne to mothers with FHF had clinical course resembling FHF as against 2 (10%) of the 10 HEV infected babies borne to mothers with nonfulminant disease (p=0.008). Table 2 compares the maternal and obstetric characteristics of women with FHF who survived (n=6) and those who died (n=10). The 2 groups had similar clinical and biochemical parameters. However, pregnant women who died had more severe cerebral edema than those who survived (p=0.002). The babies borne to mothers who survived had less severe liver disease and only 3 (50%) of the 6 such babies had FHF as compared to 9 (90%) of the 10 babies borne to mothers who died (p=0.10). In addition, mothers with FHF who survived had shorter duration between onsets of encephalopathy to delivery than those who died (2.3 ±1.0 vs. 9.6± 3.0; p=0.02). In fact, all the 6 pregnant women who survived delivered babies within 4 days of onset of encephalopathy. Such mothers had rapid clinical improvement soon after the delivery of the baby. Of the 10 pregnant women who died, 7 presented with FHF and another 3 developed FHF during the hospital course while they were carrying undelivered fetuses with severe HEV infection and all these babies at birth had evidence of FHF. Nine (75%) of the 12 mothers with FHF who gave birth to babies with FHF had DIC complicating the clinical course of their illness as against none of the 4 mothers who gave birth to healthy (n=1) or

icteric HEV babies(n=3) ($p<0.01$).

Discussion

In the present study, we followed a cohort of 36 pregnant women with HEV infection. Sixteen women either presented with FHF or developed FHF during hospital course. Increased severity of viral hepatitis in pregnant women had been reported from the Indian subcontinent, Iran and many other developing countries [12,13,14]. These data were looked upon with skepticism as selection bias could not be ruled out in the hospital data which formed the basis of these reports. Data collected from an outbreak of hepatitis E in Kashmir (1981) showed that the frequency of hepatitis was greater in pregnant (17.3%) that in non-pregnant (2.1%) women and in men (2.8%)[7]. The frequency of the disease in the first, second and third trimesters were 8.8%, 19.4% and 18.6% respectively. Severe disease in the form of fulminant hepatic failure developed more often in pregnant women (22.2%) that in non-pregnant women, none of whom had this complication, and in men (2.8%). Fulminant hepatitis developed exclusively in the third trimester. The overall mortality in pregnant women was found to be 20%. The nutritional status of women in the area affected by the outbreak or those women who developed fulminant hepatic failure was assessed as good. Since then, a number of reports have identified pregnancy especially second and third trimester as a high risk for development of FHF during epidemic as well as sporadic HEV infections[8,15,16,17].

Vertical HEV infection (mother-to-fetus) was diagnosed in 25 of the 36 pregnant women in the present study. The liver disease in the babies borne with vertically transmitted HEV infection was severe and 14 (60.9%) of 23 babies with icteric HEV infection developed a syndrome of fatal FHF. In an earlier study we studied eight babies born to mothers infected with HEV infection in third trimester. Six infants had evidence of vertically transmitted HEV infection[16]. One baby had icteric hepatitis at birth and four babies had anicteric hepatitis. Two babies had FHF at birth and presented with hypothermia and hypoglycemia and died within 24 h of birth. From our earlier observations and those of the present study we conclude that HEV is commonly transmitted from infected mothers to their babies with significant perinatal morbidity and mortality. Similar observations have been made in another study from the Middle East[11].

The data from this study point to definite relationship between FHF of the infants and mother. Twelve (75%) of the 16 pregnant women with FHF delivered babies with fatal FHF. Another 3 babies had icteric hepatitis and only one healthy baby was borne to this group. The severe fetal disease could be a cause or effect of the severe maternal disease. Mothers with severe HEV infection may transmit the disease to the fetuses and this could be related to increased viral load or prolonged viremia in the mother.

However we believe that fetal disease influenced the course of maternal HEV infection. First, mothers, with FHF who survived have less severe fetal liver disease as against those who died. Second, there was a strong correlation between severity of liver disease in the fetus and occurrence of DIC in the mother. Although DIC can occur in patients with FHF, it's occurrence in a high percentage of mothers (9/12; 75%) with severe fetal HEV infection and none (0/4) in patients with no or mild fetal HEV infection strongly pointed to the causal relationship of severe HEV infection in the fetus to DIC in the mother. Third, all 6 mothers with FHF who delivered in the first 4 days (2.3±1.0 days) of the onset of encephalopathy survived. In contrast 10 mothers with FHF who had delivered much later after onset of encephalopathy (9.6±3.0 days) died. This led us to believe that fetuses with severe hepatitis caused by vertically transmitted HEV infection were related to outcome of FHF in the mothers. If so, how is fetal FHF related to maternal FHF? This relationship was akin to what happens in mirror syndrome in which mother develops generalized anasarca subsequent to fetal and/or placental edema[18,19,20].

The possible mechanism of increased severity of liver

Table 1. Comparison of various parameters of mothers and infants between patients with nonfulminant and fulminant hepatic failure. All figures are number of patients Unless otherwise specified.

	Nonfulminant	Fluminant	P value
Number of Women	20	16	
Maternal event			
Age-mean ± 1SD (range) Years	24.7±4.4 (21-36)	29.0±6.0 (20-40)	0.11
Trimester			0.35
First	1	0	
Second	2	4	
Third	17	12	
Serum bilirubin- mean ± ISD, (range), md/dl	9.2± 6.5 (3-24)	14.7± 6.9 (6-33)	0.09
ALT-mean± 1SD, (range), IU/I	387± 436 (1110-1670)	616± 376 (118-1216)	0.19
HEV RNA reactive	6	6	0.63
Obstetric events			
Type of delivery			0.25
Aborted	3	0	
Premature delivery	4	3	
Full term	13	13	
HEV Status of infants			0.004
Not infected	10	1	
Infected	10	15	
HEV RNA +	5	15	<0.001
Clinical disease in infants			<0.008
Anicteric HEV	2	0	
Icteric HEV	6	3	
Fulminant HEV	2	12	
Serum bilirubin-mean ± 1SD,(range), mg/dl	5.3± 5.8 (1-18)	7.8± 3.7 (1-15)	0.12
ALT-mean± 1SD, (Range),IU/l	97± 5.8 (23-199)	305± 165 (51-650)	0.002

Table 2. Comparison of various parameters of mothers and infants between Patients with fulminant hepatic failure who died and survived. All figures are number of patients Unless otherwise specified.

	Fluminant		P value
	Survived	dead	
Number of Women	6	10	
Age-mean ± 1SD (range) Years	33.7±5.5 (26-40)	26.2±4.5 (20-35)	0.11
Trimester			0.55
First	0	0	
Second	2	2	
Third	4	8	
Hepatic encephalopathy			
Grade-mean±1SD	3.0±0.89	3.5±0.53	0.26
Number with grade 1 or 2	2	0	0.05
Number with grade 3 or 4	4	10	
Cerebral edema	2	10	0.002
DIC	3	6	0.69
Serum bilirubin- mean ± ISD,	13.3± 6.1	15.5± 7.6	0.25
(range), mg/dl	(6-23)	(9.0-33.0)	
ALT-mean± 1SD, (range),	638± 388	602± 388	0.46
IU/I	(163-1160)	(118-1216)	
HEV RNA reactive	4	2	0.06
Obstetric events			
Type of delivery			0.86
Aborted	0	0	
Premature delivery	1	2	
Full term	5	8	
Onset of encephalopathy to delivery (Days)	2.3±1.0 (1-4)	9.6±3.0 (5-14)	0.02
HEV Status of infants			0.18
Not infected	1	0	
Infected	5	10	
HEV RNA +	5	10	0.18
Clinical disease in infants			0.17
Anicteric HEV	0	0	
Icteric HEV	2	1	
Fulminant HEV	3	9	
Serum bilirubin-mean ± 1SD,(range), mg/dl	5.3±3.3 (1-11)	9.4± 3.1 (5-15)	0.25
ALT-mean± 1SD, (Range),IU/l	221± 145 (51-432)	361± 160 (123-650)	0.24

disease in the mother may be due production of toxic metabolites in the fetus with FHF. Such toxins can cross over to maternal blood and precipitate onset of hepatic encephalopathy and possibly DIC in the mother with HEV infection. Such a mechanism has been established for the pathogenesis of acute fatty liver of pregnancy (AFLP) in which fetus is homozygous for long-chain-3-hydroxyacyl-CoA dehydrogenase (LCHAD) deficiency and produces large amounts of toxic omega fatty acids, which cross over to the maternal blood [3]. Such toxic fatty acids overwhelm the mitochondrial-oxidation machinery of the heterozygous mother, who is already under stress from the increased demand for fatty acid oxidation in the latter stages of pregnancy. Microvesicular steatosis, DIC and FHF are dominant features of AFLP and immediate termination of pregnancy is indicated in this clinical syndrome. This leads to rapid improvement in the maternal disease.

Further studies are needed to substantiate this hypothesis. Severity of fetal disease in utero can be assessed by examination of the amniotic fluid or fetal blood sampling and correlated with the maternal disease. Mechanism by which fetal HEV infections can affect maternal HEV disease needs to be studied. Randomized studies between immediate termination of pregnancy and expectant approach about delivery are urgently needed to assess their effect on outcome of the mother. Up until now clinicians believe that immediate termination of pregnancy may add additional stress to mother and lead to higher mortality. However, this is not based on any data or studies.

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Do all Fibroadenomas Needs Surgical Excision?

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Abstract

Fibroadenoma is a common cause of discrete breast lumps in young females. The traditional management remains the surgical excision of all the fibroadenomas in the belief that it may harbor a carcinoma but this viewpoint is being questioned. The present study reviews the management of 113 cases. Their mean age was 23.6, average tumour size of 2.1 cm and single lesion was the commonest presentation. The final histopathology did not reveal a single case of coincident in-situ or infiltrating carcinoma within the fibroadenoma among the 106 cases of excision biopsy. Today, when confident diagnosis is possible with triple assessment; as an alternative to excising all benign breast lumps, diagnosed fibroadenomas can be managed conservatively, since they have no inherent premalignant potential and there is a prospect of spontaneous regression. However, all breast lesions above 5 cm in size or rapidly increasing in size, patient above 30 years of age and with uncertain diagnosis should be excised.

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Introduction:

Fibroadenomas are the commonest benign breast lesions[1] that account for 50% of all breast biopsies[2] and up to 75% of biopsies in women under the age of 20 years.[3] Fibroadenomas were previously recognized as benign tumours of breast[4] but are now considered to be aberrations of normal development rather than neoplasms.[5] The reason is that fibroadenomas develop from a whole breast lobule, which is contrary to the origin of neoplasm from a single cell with evidence of proliferation of both connective tissue and lobular epithelium. Histologically, fibroadenomas resemble a hyperplastic breast lobule and they also respond to same hormonal stimuli as the normal breast tissue.[6] The biological behavior of fibroadenoma is unpredictable; they may regress, remain static or grow progressively. Fibroadenomas per se are not premalignant and any association with malignancy if any is unfounded. Furthermore, Triple assessment that is used routinely in evaluation of breast masses has made the accurate preoperative diagnosis a reality. In the current scenario of better understanding and improved diagnosis one has to question that "Do all fibroadenomas needs surgical excision" and what are the pros and cons of not removing them. The present study was undertaken to evaluate our current practice and to define the best management strategy for this common clinical condition.

Materials and Methods:

Retrospective review of medical records of all the patients who were diagnosed as fibroadenoma or benign lesion and treated at Riyadh medical Complex from 1st July 2002 to 30th June 2005 was made. The patients above 35 years of age, tumour size of more than 5 cm and unsatisfactory cytology were excluded from the study. The age of the patient, preoperative clinical diagnosis, cytology and radiological results were recorded. The treatment performed and final histopathology report was noted. The patients who were offered conservative management were followed in outpatient department, 3 monthly in first year and biannually subsequently. This treatment was terminated by excision biopsy at the request of the patient or if the lump was increasing in size.

Results:

A total of 113 patients were treated in the 3 years period. Their ages ranged from 15-35 years with mean age of 23.6 years. The majority of patients 78(69%) were under 25 years of age. The detailed age related distribution is shown in Fig. 1. The single lesion was present in 86(76.1%) followed by bilateral in 16(14.1%) and multiple in 11(9.7%). The commonest site is upper outer quadrant in 51(45.1%) followed by central in 18(15.9%). The mean tumour size was 2.1cm, which ranged from 0.5 – 5 cm but most of the patients 95(84%) have tumour size of less than 3 cm. Only 15 patients initially agreed for conservative management but within a year 8 patients opted for surgical excision on the grounds mentioned in material and methods. Only seven patients are still continuing with conservative management with decrease is size in four cases. The correlation between preoperative assessments and final histopathology in those lesions that were excised is given in table 1. There was not a single case of carcinoma in fibroadenoma in all-106 excised lesions. The commonest

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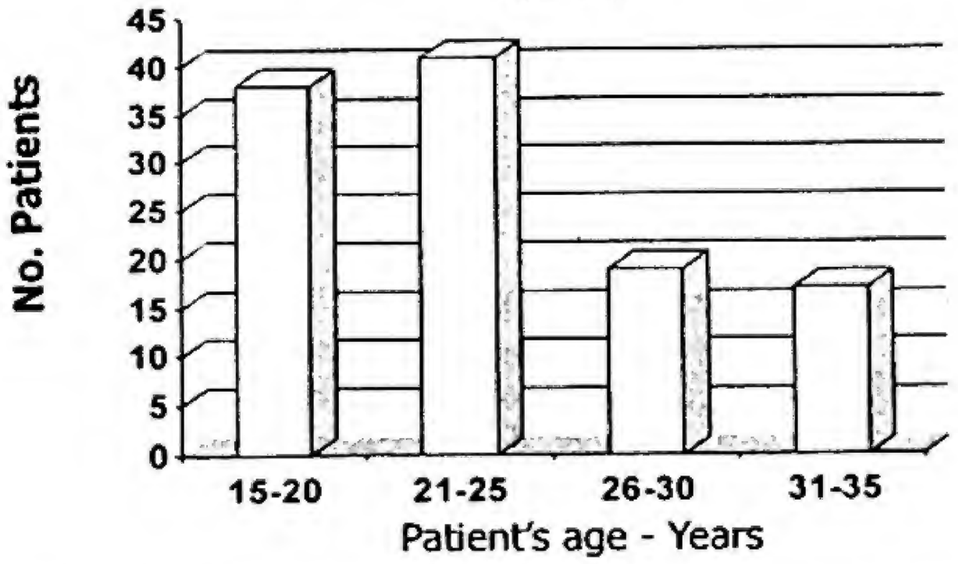
(3.8%) variation in final histopathology was other benign lesions such as fibroadenosis or fibrocystic change and benign epithelial cells.

Discussion:

Fibroadenoma is a common cause of breast lumps especially between the ages of 15-25 years.[7,8] Traditionally, all Fibroadenomas were treated by surgical excision just to exclude malignancy. The doctrine that all discrete breast lumps should be excised has recently been challenged because if confident diagnosis and exclusion of malignancy is possible with preoperative investigations than the need for excision biopsy can be obviated. The current view that fibroadenomas are hyperplastic rather than neoplastic lesions and proposed hormonal influences, it is appealing to consider fibroadenomas as an aberration of normal lobular hypertrophy during the period of maximal estrogen exposure. This concept gives support to a policy of non-surgical management.[5,9]

FIGURE-1
AGE RELATED DISTRIBUTION
N= 113



The classical clinical features of fibroadenoma such as discrete, smooth, very mobile and non-tender may not be enough for a firm scientific diagnosis.[10] Imaging, mainly ultrasonographic examination alone in this age group alone is rather disappointing. The present study showed the accuracy rate of 81.8% that is quite similar to the most of reported studies,[11] although some studies has reported upto100% when all benign criteria are met.[12] Ultrasound is very accurate method in assessing and monitoring the size of the lesion. Unfortunately ultrasonography was used in a small fraction of case, as the main treatment mode in our hospital is still surgical excision. Mammography is only rarely indicated in very high-risk cases especially above 30 years of age. Cytology is the most useful test for the diagnosis of fibroadenoma with reported positive predictive value of 95%,[13] which was observed in present study (93.4%) as well. But, the present evaluation of all breast masses by a combination of clinical examination, imaging and cytology (Triple assessment) has made a confident diagnosis possible. When all components of the triple test show benign results in a patient of fibroadenoma, the diagnostic accuracy reaches 99.6%, hence the chance of false negative diagnosis is very low.[14] However, if any of these test shows suspicion of malignancy or even an inadequate cytology, it becomes an indication for excision or core biopsy to obtain a histological diagnosis.[15]

Despite the fact that the natural history of fibroadenomas remains uncertain but the possibility of spontaneous regression is there. Haagensen believed that most fibroadenoma grew to 1-2cm in size and than remain unchanged.[16] The reported rate of spontaneous resolution of fibroadenoma over a period of 1-5 years varies between 16-50% and another 12% decrease in size.[17,18] Moreover, 50-70% remain unchanged in size and only 7-8% will increase in size, therefore require excision biopsy.[19] Why fibroadenomas regress is not clear but, it has been observed they progressively lose cellularity with age.[20]

Fear of cancer and death is an overriding concern in women with breast tumours and is a prime driving force for excision. To make the non-surgical management of fibroadenoma an acceptable treatment option one has to answer the question that what is the risk of leaving or risk of developing carcinoma in fibroadenoma and secondly, medicolegal implication of a wrong diagnosis or delay in diagnosis of breast cancer. The first question has been answered in many studies, as well as observed in present study that among the 106 excised cases not a single case proved to be a carcinoma. This is widely accepted now that fibroadenomas are not a risk factor for carcinoma. The reported incidence of carcinoma or malignant change varies from 0.02 to 0.3%, usually to lobular carcinoma insitu.[21,22] Furthermore, most of theses reported carcinoma have been seen in women above 35years of age and this has been suggested as the cut- off age for conservative management of fibroadenomas .[23] The reported cut-off age varies from 25 –35 years. The age of 30 years seems a reasonable choice allowing 85% of patients in present study to be considered for conservative management.[5] Regarding the medico-legal aspect, it is mandatory that conservative management be only offered to patients in which all components of triple tests confirms benign pathology, patients signs informed consent knowing the limitations of the test and a clear follow-up plan is decided.

Although, excision of the lesion is a definitive solution but involves unnecessary excision of benign lesions, cosmetic issues and above all place an enormous burden on healthcare system. At the same time one can question the need for removal of a harmless lesion when confident exclusion of malignancy is possible in present era. Although, our experience in non-surgical management of fibroadenoma is still at infancy stage and majority of patients 8/15 opted for surgical treatment within a year but in only 2 patients has the fibroadenoma actually increased in size. Others have observed this phenomenon as well[24] but there are growing number of studies with encouraging results and long-term follow-up (5-9 years) on conservative management of fibroadenomas.[25,26] This highlights the need for patient education and to develop(patient's confidence on conservative management of such benign lesions, which can only come with growing number of patients on conservative therapy.

Hence, as fibroadenomas are completely benign and do not carry a risk of malignancy especially in women less than 30 years of age, the non-operative management seems a viable option. However, it is emphasized that further clinical research is required to assess the safety and to evaluate the potential economic gain as well as the benefit of decreased physical and emotional trauma to the patient.

Table -1 : Correlation Between Pre-operative Investigations & Final Histology(N=106)

Category	Cytology N (%age)	U/S N (%age)	Mammogram N (%age)	Histopathology N (%age)
Performed	106 (100%)	33 (31.11)	05 (4.7%)	106 (100%)
Fibroadenoma	99 (93. 4%)	27 (81.8%)	03 (60%)	95 (89.6%)
Fibroadenosis / Fibrocystic Dis.	04 (3.8%)	02 (6.0%)	01 (20%)	08 (7.5)
Benign	02 (1.9%)	04 (12.1%)	01 (20%)	03 (2.8)
Normal tissue	01 (0.9%)	- -	- -	- -

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original article

Hepatic Resection : The Ideal Management of Localized Caroli's Disease

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Abstract

Caroli's disease is a rare disease and has remained under-diagnosed in the past. Improved imaging modalities have increased the prospects of diagnosing Caroli's disease. The condition is still quite often treated improperly due to lack of experience owing to the rarity of the pathology.

Present study was undertaken to evaluate our experience and the role of hepatic resection in the management of Caroli's disease. Fourteen cases of Caroli's disease managed during the last 15 years were analyzed for clinical presentation, diagnosis, management and outcome. The disease was localized to single lobe in 8 (57%) cases, out of which 7 underwent successful hepatic resection and all remained symptom free after the surgery. The remaining 6(43%) cases with diffuse disease remains a therapeutic challenge. One of these patients with associated congenital hepatic fibrosis presented with persistent haematemesis and underwent emergency modified Sugiura's operation. Symptomatic control was achieved by repeated endoscopic clearances in the remaining 5 cases.

Hence, We conclude that hepatic resection remains the treatment of choice for localized disease and provides a chance of cure. The overall prognosis of diffuse disease remains poor and liver transplantation may be regarded as the only hope for cure.

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Introduction:

Caroli's disease is a rare autosomal recessive, hereditary disorder characterized by congenital saccular dilatations of the intrahepatic bile ducts involving a segment, a sector, a lobe, or whole of the liver. Vachell and Steven[1] first described the disease in 1906 but the detailed description of the disease came from Caroli and Couihaud[2] in 1958, and hence, carries the name Caroli's disease. It consists of 2 types: pure or simple, with bile duct dilatation or ectasia alone, and periportal fibrosis or complex, with associated congenital hepatic fibrosis (CHF) and portal hypertension.[3] Both types in many cases are associated with nephrospongiosis (benign renal tubular ectasia) or Cacchi-Ricci's disease.[4,5] The association with CHF and renal malformations may justify the use of the term Caroli's syndrome.

Caroli's disease, though congenital, but presentation is usually delayed for many years.[6] Stenosis and dilatations of bile ducts lead to biliary stasis with resulting intra-hepatic biliary lithiasis. If left untreated, recurrent suppurative cholangitis, intra and extrahepatic abscesses often lead to fatal septicemia,[7,8] and occasionally cholangiocarcinoma in long standing cases.[9] In periportal fibrosis type, the signs and symptoms of portal hypertension dominate the picture. Although the disease is rare but is recognized more frequently now a day because of improved hepatobiliary imaging techniques. Despite the sporadic case reports no standard treatment strategy is applied world over. The commonly used procedure, like bilio-digestive anastomosis and repeated ERCP clearances are often unsuccessful and more so fail to provide permanent cure.[8,9] The ideal treatment would be one which provides complete relief of symptoms and prevents the development of fatal complications. Over last 15 years, we came across a varied spectrum of Caroli's disease in 14 patients with successful hepatic resection in 7 cases. The present study is prompted by the fact as it presents a good number of cases, considering the rarity of disease, and highlights the place of hepatic resection in management of CD.

Material and Methods:

Since 1988, the authors have managed 14 cases of recurrent cholangitis, who were finally diagnosed as Caroli's disease. The study was undertaken after approval of research and ethical community of the hospital. All, except one case, presented with recurrent attacks of right upper quadrant abdominal pain, vomiting, fever with chills & rigors and jaundice. One 11 years old girl presented with repeated bouts of haematemesis and melaena for 6 months. She was found to have ascites, massive hepatosplenomegaly and features of hypersplenism, grade III esophageal varices and nephrospongiosis. Apart from the hematological investigations, the basic diagnostic work up consisted of abdominal ultrasonography (US), computed tomography (CT) and ERCP (endoscopic retrograde cholangiopancreatography). High-pressure intra-

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operative cholangiography and percutaneous transhepatic cholangiography (PTC) were used where indicated. An upper GI endoscopy was carried out in one case of haematemesis.

The diagnosis of CD was made on basis of recurrent episodes of cholangitis, presence of intrahepatic stones, usually in absence of gallbladder and common bile duct stones, and typical radiological changes in intrahepatic bile ducts such as, multiple strictures with segmental cystic dilatations and retrieved stone analysis showing pigment (bilirubinate) stones. Final confirmation was made on histopathology of the resected liver specimen in cases of hepatic resection and liver biopsy in one case of CHF. The classical microscopic feature of CD is an ectasia of the intrahepatic bile ducts resulting in focal cystic dilatations separated by segments of nearly normal looking bile ducts. The epithelial lining is cuboidal with frank papillomatous appearance, like that of gallbladder, and containing bilirubin calculi. Another striking feature is the absence of any abnormality in hepatic lobules and a normal parenchyma surrounding the ducts. The characteristic lesions are found in large portal spaces that affect only the segmental bile ducts with infiltration of portal triads with mononuclear and polymorphonuclear cells but having no effect on the portal system in simple type of CD. Enlarged portal triads with abundant connective tissue and foci of bile ductules proliferation are present in cases associated with CHF. This type involves portal system consequently leading to changes of portal hypertension.

The initial management consisted of nasogastric aspiration, correction of fluid and electrolyte balance, broad-spectrum antibiotics, analgesia and correction of anemia and coagulation profile, where indicated. After basic diagnostic work up, endoscopic papillotomy with clearance of intrahepatic stones was tried and in case of failure of complete clearance, nasobiliary drainage was carried out to decompress the biliary tree. Once the cholangitis was controlled each case was evaluated and treatment option was individualized for every patient. The resected specimen of liver was sent for histopathology and stones were sent for analysis and microscopic examination to exclude the ova or parasites in the stone (Ascaris lumbricoides or Clonorchis sinensis). The cases diagnosed as Asiatic cholangitis were excluded from the study.

All operated cases were provided with standard post-operative care and monitored for any complication during the hospital stay, which was treated accordingly. All patients were regularly followed in outpatient's clinic and check ERCP was performed in first two cases of hepatic resection at 6 months to 1-year period during the follow-up.

Results:

A total of 14 patients with the final diagnosis of CD were managed at Riyadh Central Hospital, Riyadh, Saudi Arabia, from 1988 to 2003. They were 9 males and 5 females with male to female ratio of 1.8:1. Only 2 were local residents and rest 12 were

Table No. 1 : Age, Sex, Disease pattern, operation performed & outcome

No.	Age/Sex	Dis. Pattern	Operative procedure	Follow-up/ Duration
1	20yrs/M	Left lobe	1.cholecystectomy, extended choledochotomy & sphincteroplasty 2.Left hepatic lobectomy	Symptom free 4yrs
2	42yrs/M	Left lobe	1.Left hepatic lobectomy, Choledochoduodenostomy& Cholecystectomy 2.T.vagotomy, pyloric exclu. & Roux-en-Y gasterojej.	Symptom free 3 yrs
3	37yrs/M	Both lobes	Repeated ERCP clearances	Symptomatic control, 9 months
4	50yrs/M	Left lobe	Left hepatic lobectomy	Symptom free 6yrs
5	30yrs/F	Left lobe	Left hepatic lobectomy	Symptom free 3 months
6	11yrs/F	CD with CHF & Nephrospongiosis portal hyperten.	Liver biopsy, Modified Sugiura's operation	Good control of haematemesis
7	37yrs/M	Rt. lobe	Repeated ERCP clearances	Symptomatic control
8	27yrs/F	Both lobes	Pt. refused fo r resection Initial management & ERCP clearances	Went back to her country
9	40yrs/F	Both lobes	Repeated ERCP clearances 3 times in 2yrs	Symptomatic control, 2yrs
10	37yrs/M	Segmental (II&III)	Segment II & III resection Cholecystectomy and CBD exploration in other hosp.	Symptom free 2yrs
11	32yrs/M	Left lobe	Left hepatic lobectomy	Symptom free 1yr
12	60yrs/F	Both lobes	Cholecystectomy & CBD exploration in other hosp. Repeated ERCP clearances	Symptomatic control, 6yrs
13	35yrs/M	Both lobes	Cholecystectomy 4yrs ago ERCP, refused treatment.	Went back to his country
14	29yrs/M	Left lobe	Left hepatic lobectomy	Symptom free 3yrs

foreigners; this distribution may be related to prevalence of the disease in these parts of the world. The age ranged from 11-60 years (mean 34.8 (±12) years). The age, sex, disease pattern, operative procedures performed, outcome and follow-up period are shown in Table I.

The disease was localized in 8 (57%) cases, while diffuse in 5 (35.7%) and 1 (7.1%) case has CHF with predominant features of portal hypertension. The patients with localized disease (8) were considered suitable for hepatic resection; left lobectomy was performed successfully in 6 cases (Fig. I showing resected lobe of liver with intrahepatic stones) and segmental (segment II&III) resection in one, whereas one case involving right lobe refused surgery. The specimen histopathology confirmed the diagnosis of CD and none of the stones showed any evidence of parasitic infestation on microscopy.

One patient of diffuse CD with CHF presented with repeated episodes of haematemesis. This young girl underwent emergency modified Sugiura's operation (Splenectomy, Gastroesophageal devascularization and esophageal transaction) to control relentless bleeding in spite of repeated sclerothrapies. The open liver biopsy confirmed the diagnosis of Caroli's disease with associated congenital hepatic fibrosis. She was subsequently referred for liver transplantation. Among the remaining 5 patients of diffuse disease, one 60 yrs old local female in addition to outpatient visits and treatment had five admissions with cholangitis since her diagnosis 6yrs ago, every time treated with antibiotics and ERCP clearance. She was referred for hepatic transplant but because of her age (63yrs) and cardiac disease was refused for transplant. All other patients of diffuse disease including young girl with CHF were advised for transplantation but because of non-availability in early part of study or eligibility problems were unable to have transplantation and left to their native countries.

There was one intra-operative complication, iatrogenic injury to right hepatic duct that was identified during operation and repaired over T-tube. The patient had smooth post-operative course and had normal postoperative T-tube cholangiogram. T-tube was removed and patient was discharged 5 weeks post-operatively in good condition. There was no postoperative mortality. The commonest postoperative complication was chest infection in 2 cases, which was minor and self-limiting managed by chest physiotherapy. Among the delayed complications, one patient who had choledochoduodenostomy developed persistent epigastric pain, which on endoscopy found to have severe antral biliary gastritis. This patient ultimately required truncal vagotomy, pyloric exclusion and Roux-en-Y gasterojejunostomy two years after the first operation and remained symptom free ever since.

Follow-up ranged from 3 months to maximum of 6 yrs with average follow-up of 2.75 years. The overall symptom control was good and complete cure was achieved in all cases of hepatic resection. In spite of a very long study period, our follow up is not long enough due to a simple reason that all of the hepatic resection cases were non-residents and due to their migration we were unable to maintain a long follow up with them.

Discussion:

The Caroli's disease is a rare disease, with an estimated incidence of 1/1,000,000 cases.[10] Owing to the rarity of disorder, the diagnosis is often delayed and lack of experience frequently results in inappropriate treatment. The typical presentation of disease by recurrent attacks of pain, fever and jaundice draws all attention to common bile duct, resulting in futile operations (Cholecystectomy, choledochotomy, sphincteroplasty and biliodigestive anastomosis) on CBD, as observed in world literature[10,11] and also we did in our first case. That's why, it is said that always remember the intrahepatic lithiasis (Caroli's disease) if extrahepatic biliary tree is normal in a classical case of cholangitis.[10-12]

The current generation of diagnostic modalities has almost solved the problem of diagnosis. Today the pre-surgical diagnosis of CD can be established confidently with abdominal ultrasonography (US) and computed tomography (CT). The diagnostic US and CT features are multiple cystic dilatations of intrahepatic bile ducts which sometimes partially or completely surround the portal radicles giving rise to so called central dot sign.[11,13-15] In addition, the associated lesions in other organs can also be demonstrated at the same time, as shown in Figure II. In spite of the risk of introduction of infection and occasional failure to outline the lesions due to stenosis or obstruction by stones or debris, the endoscopic retrograde cholangiopancreatography (ERCP) which outline the intrahepatic biliary tree showing classical picture of multiple saccular dilatation with intervening strictures, as shown in Figure III, remains the important diagnostic tool for preoperative evaluation as well as to follow the progression of the disease.[10,11,16] Similarly the percutaneous transhepatic cholangiography (PTC) and operative cholangiography are useful diagnostic aids. Recently the use of magnetic resonance cholangiopancreatography (MRCP) is advised as it is free from the drawbacks of ERCP[17] but because of non-availability in our center in initial part of study, it was not used. Nuclear medicine techniques, like Technetium-99m DISIDA, have been reported as being highly sensitive, noninvasive, inexpensive and safe[18] but are nonspecific.[15] Hence, CT scan and US may be regarded as more specific and best modalities for evaluating and making the diagnosis. Invasive procedures, like ERCP and PTC, for confirmation of the diagnosis remain the corner stones for the diagnosis of CD.

Precise delineation of the disease pattern and its differentiation from other conditions are of vital significance before selecting the therapy. The disease presents in a localized and diffuse form. Later is more common and usually associated with CHF. There is strong association between CD especially one with CHF and medularly sponge kidney.[3,4,19] This was also observed in one of our cases, as shown in Fig. II. The reported incidence of localized or monolobar CD varies between 20-40% and more than 90% of these is confined to left lobe. The (57%) incidence of localized CD in present study is higher than the many reported figures.[10,20,21] Higher incidence of localized CD has also been observed by M. Mercardier et al.[19] This disparity may be due to different population under study but, to our knowledge no such study from this region is available for comparison.

The CD should be differentiated from recurrent pyogenic cholangitis (RPC), also known as cholangiohepatitis or oriental or infestational cholangitis that is quite often seen in Far East. This condition can be distinguished from CD by typical radiological appearance on ERCP which in contrast to CD involve extrahepatic biliary tree mainly CBD, CHD and left hepatic duct just above the bifurcation and stricture-dilatations with marked smooth dilatations and excessive branching of intrahepatic ducts with prominent arrow-head formation,[22-24] differentiate this from CD. In addition, hard stones, in contrast to soft stones of CD, are also mostly confined to extrahepatic ducts and in up to 50% of cases clonorchis infestation could be demonstrated. Dead clonorchis had been demonstrated in the center of stones.[23,24] Similarly Ascaris ova have been found in the stones.[24] All these evidences clearly points to infestational pathology rather than a congenital origin, hence the treatment is also different than CD.

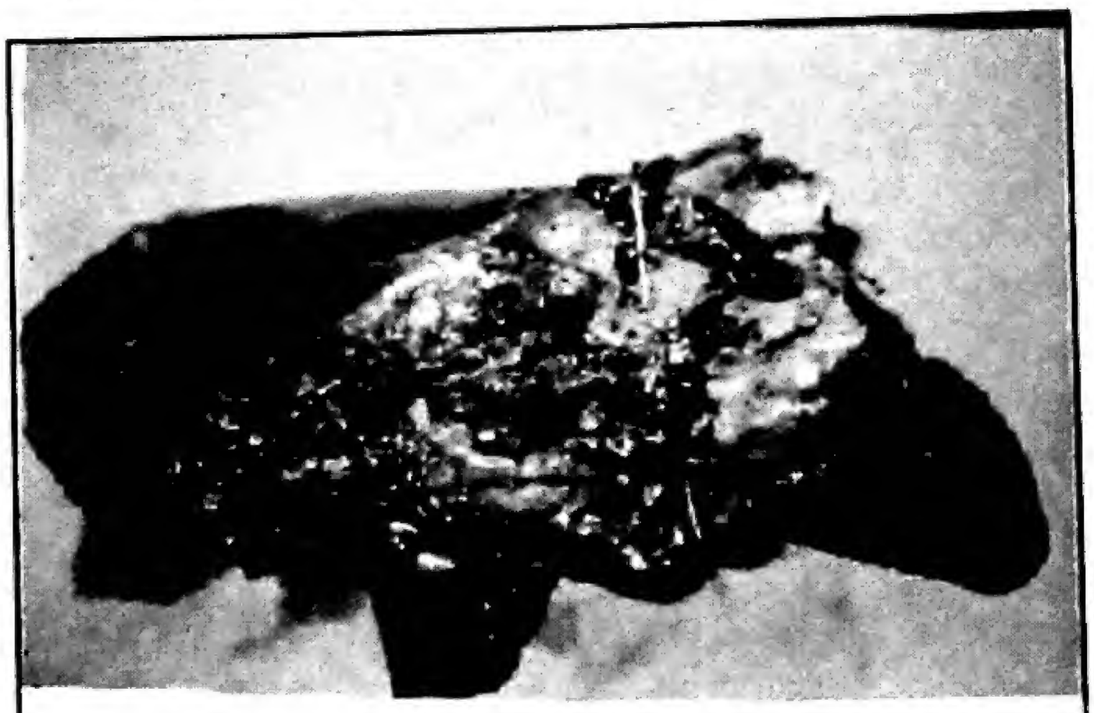
The most vital therapeutic consideration while planning the treatment of CD are cure or permanent relief of recurrent attacks of cholangitis and prevention of future development of cholangiocarcinoma. The incidence of cholangiocarcinoma is substantially high; the reported incidence varies between 7-14%.[20,25-27] The carcinoma is believed to develop when biliary epithelium is exposed to long standing inflammation due to bile stasis, hepatolithiasis and recurrent bacterial infection leading to

epithelial hyperplasia-dysplasia and eventually carcinoma.[25,26] While, a study by Parada et al[28] on liver biopsy specimen of CD (without cholangiocarcinoma) has recognized several clonal chromosomal abnormalities. Although, uncertainty remains to be clarified that whether local or genetic factors are more important in development of carcinoma, the disease carries a significant risk of cholangiocarcinoma. The risk of malignant change is supposed to be higher in monolobar disease than diffuse forms,[10] further suggesting more radical approach in localized disease. Even the squamous cell carcinoma has been reported as a complication of CD.[29,30] Considering all these problems, when feasible resection of diseased part of liver seems the most suitable treatment.

Localized forms, which are generally confined to left lobe or occasionally to right lobe of the liver, are suitable candidates for hepatic resection. Currently, such resections can be performed with minimal morbidity and mortality, as observed in present study as well as in many other studies.[11,19-21,25] Moreover, the excellent symptomatic relief during long term follow-up, as noticed in our cases of hepatic resection and also validated by others[11,31] and eliminating the potential site for developing carcinoma[20] uphold this therapeutic management. Such appropriate treatment is still often undertaken on a secondary basis either because of wrong initial diagnosis or when disease is recognized but inappropriately treated by sphincteroplasty or bilioenteric drainage procedures.[21,32] We admit that we too did the same mistake in our first case and also added unnecessary drainage procedure in second case to safeguard the development of disease in the remaining liver which ultimately ended up in second operation. Furthermore, two of our cases had such operations in other hospitals before referral to us. This highlights the need for awareness about this pathology and its management strategies.

Panhepatic or diffuse forms of CD continues to be a greatest therapeutic challenge. Many types of external and internal drainage procedures have been tried but with limited success. The permanent external drainage method like Praderi's operation [33] or internal drainage procedures such as, Sphincteroplasty, Choledochoduodenostomy are not only ineffective but also attended by ascending cholangitis, thus should be avoided.[34,11,19] Long limb Roux-en-Y choledochojejunostomy or hepaticojejunostomy are the favored method of internal drainage for CD and have lower incidence of such a risk[19, 32] All these procedures remain inefficient due to specific pathology of CD, multiple intrahepatic stricture-dilations making these as inefficient drainage procedure.[11,35] Mercadier has combined left sided resection with disimpaction of stones in right half of the liver and Roux-en-Y hepaticojejunostomy.[19] Finally, permanent access hepaticojejunostomy, in which closed end of loop of Roux-en-Y hepaticojejunostomy is buried subcutaneously for ready access for ERCP or choledochoscopy and intermittent lavage of the diseased liver on an outpatient basis has been reported with good symptomatic control.[36,37] For our own part, we did not use any of the above drainage procedures, as we believe that none of the above procedure provides permanent relief of symptoms or cure.[11,19,36,37] Our reliance was mainly on endoscopic removal of intrahepatic stones using dormia basket or forgarty ballon catheters under cholangiographic control. Meticulous repeated clearance of ducts with prolonged antibiotic courses enabled us to achieve a worthwhile period of symptomatic control.[11,19,38] However, the quality of life of these patients is severely impaired and long term survival remains poor.[19,35] The patient with associated CHF, complicated by portal hypertension the picture is even more gloomy.[21] The variceal bleeding should be managed by sclerotherapy or variceal banding but in case of failure of these methods, one should avoid shunt operations in patients who are possible candidates for liver transplantation.[19] For the same reason, modified Sugiura's operation was performed in our case. The only permanent cure in cases of diffuse CD is the liver transplantation[10,21,27,40], that is why we did not use any major surgical intervention in these cases and relied on temporizing measures while waiting for liver transplantation.

Hence, it is concluded that where feasible, hepatic resections is the ideal management of localized Caroli's Disease, which is not only safe but also provides the best chance of cure. Nonetheless, diffuse disease carries the poor prognosis and liver transplantation is the only hope for cure.



Resected specimen of left lobe of liver, cut section showing Intrahepatic stones

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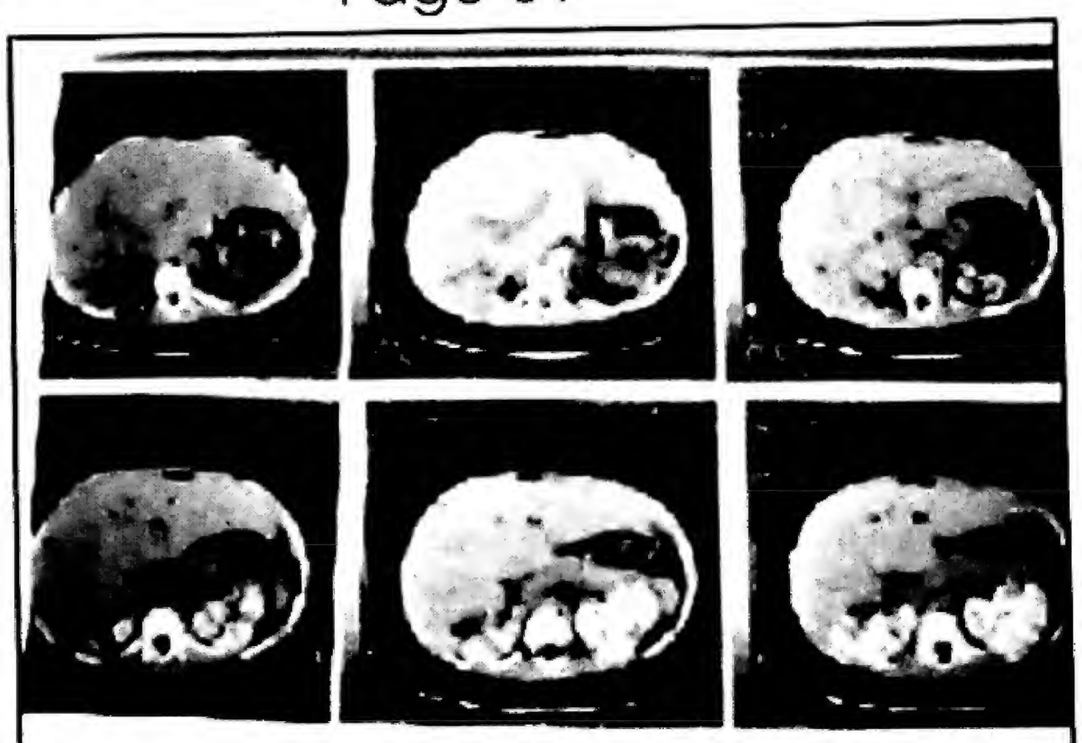

CT scan showing dilated intrahepatic ducts and nephrospongiosis

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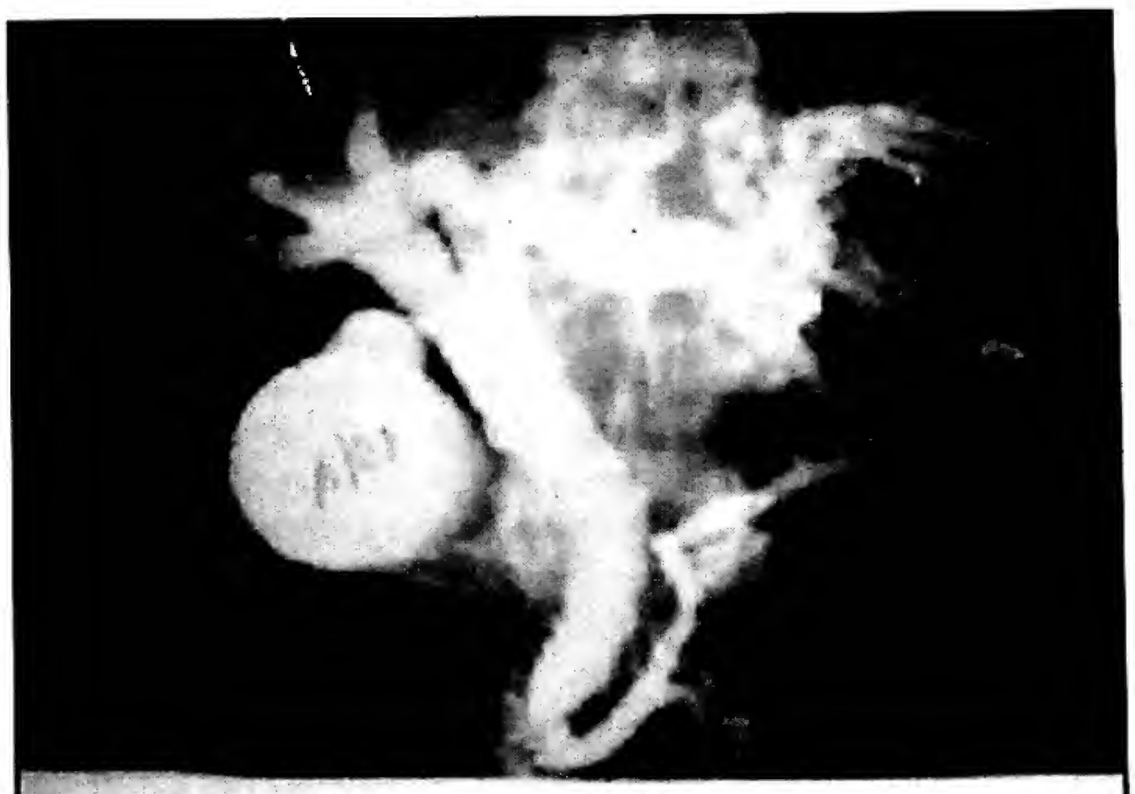

ERCP. Showing Caroli's disease, multiple stricture dilatations with intrahepatic stones confined to left lobe of liver

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Clinical experience with Tuberculous lymphadenitis in Central Saudi Arabia

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Abstract

The objective of the study was to describe the presentation, management and outcome of tuberculous lymphadenitis (TBLA) in Central Saudi Arabia.Patients with a diagnosis of TBLA who presented to Riyadh Medical Complex over a three-year period from July 2001, to June 2004 were included. Data collected included demographic, clinic al, laboratory parameters at presentation and follow up visits. One hundred and thirty five patients were included in the study with a mean age of 33.2years. Females composed 76.9% and non-Saudi nationals 58.5% - a majority of whom were from South -East Asia. Swelling was the most frequent reason for seeking medical help (79.3%) but a substantial number of patients had fever (34.1%), weight loss (13.3%) or night sweats (15.6%). Median duration of symptoms was 60 days. Localized lymphadenopathy was the most common presentation occurring in 85.93% of patients while generalized lymphadenopathy occurred in 5.93%. The cervical group was the only site involved in 70 (51.9 %) patients. Organomegaly in the form of either spleno- or hepatomegaly occurred in 31.2% of patients' Iron deficiency anaemia occurred commonly and erythrocyte sedimentation rate was normal in 13.33%. Tuberculin Skin Test and the chest radiograph were abnormal in 90.33% and, 31.9% of patients respectively. None of the patients tested for HIV was positive for the virus. All patients recorded an increase in weight at the end of therapy, which consisted of WHO category 10 schedules. Treatment related hepatitis occurred in 5(3.7%), paradoxical increase size of nodes in 8(5.9%) and residual lymphadenopathy in 23 (17.0%). TBLA in Saudi Arabia is predominantly a disease of females and occurs more often among the expatriates. Although HIV-seropositivity is rare in this group, constitutional symptoms and associated organomegaly are common features. Treatment failure is uncommon and most patients record weight gain as a response to therapy.

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INTRODUCTION:

Tuberculosis remains a major problem in the developing world and continues to cause significant morbidity and mortality. Tuberculous lymphadenitis (TBLA) is perhaps the commonest cause of extra pulmonary lymphadenitis worldwide. While its significance as a cause of lymphadenitis varies from one part of the World to another, it is certainly the commonest cause in the developing world as well as among the immigrant population in the developed world. With the emergence of the human immunodeficiency virus (HIV), there are descriptions of variations in the presentation and outcome of TBLA especially among those infected with the virus. Saudi Arabia has very low prevalence of HIV infection but high incidence of tuberculosis. TBLA is not only the commonest form of extra pulmonary tuberculosis [1,2] but also the commonest lymphadenopathy in adults in Saudi Arabia [3]. There are, however, studies describing the pattern of this disease in the Kingdom [4,5]. The study was aimed at describing the presentation, management and TBLA in a population with low prevalence for HIV infection.

MATERIALS AND METHODS:

This was a descriptive observational study in which patients aged 15 years and over seen at Riyadh Medical Complex, Riyadh, Central Saudi Arabia and diagnosed to have tuberculous lymphadenopathy between the periods of July 2001 and June 2004 were seen and followed up. Demographic, clinical, radiographic, and laboratory data were recorded. Patients were followed up for the duration of therapy and the progress of disease and side effects of medications were documented. Diagnosis of tuberculous lymphadenopathy was entertained if there were acid fast-bacilli and/ or caseating granuloma on histology or culture of lymph node biopsy material. Lymph node material was obtained by either fine-needle aspiration (FNA), excisional or open biopsy. Tuberculin skin test (TST) was carried out by intradermal injection of 5 units of purified protein derivative (PPD). All patients received WHO category I treatment schedule i.e. a combination of isoniazid, rifampicin ethambutol and pyrazinamide, the latter two drugs for the first two months and the first two for a total of at least six months. During follow up, note was taken of the patients' symptoms, weight temperature, size and number of nodes and liver function tests. Patients were excluded if follow up was incomplete. All follow up was by author (AAA). Data was analyzed using the descriptive statistical module of Statistical Package for Social Sciences (SPSS) for Windows version 12. Means and standard deviation (SD) were used to summarize continuous variables while percentages were used for categorical variables. Chi-square test was used to investigate the statistical significance between two

Keywords: Lymphadenitis, lymphadenopathy, tuberculosis

categorical variables. The level of significance chosen was 5%.

RESULT:

There were 135 patients followed up till completion of therapy. Eighteen patients were lost to follow up. The mean age was 33.3 years (SD = 11.7) with Saudi patients being significantly older than the non-Saudi patients (p = 0.0577). Similarly, average age of male patients was significantly higher than that of females (38.6 years vs. 31.5years; p = 0.0028). The female/male ratio was 3.2:1. This was more pronounced among the expatriate population at approximately 5:1. Fifty-six (41'5%) were Saudi nationals and79 (58.5%) non-Saudi nationals. The most common presenting symptom was swelling at the site of the involved node(s) occurring in 107 (79.3%) of patients. Females were more likely to present with this symptom than males (p = 0.0152). Table 1 gives the details of the presenting symptoms and shows that constitutional symptoms are not that infrequent. The median duration of symptoms at presentation was 60 days (range 2 to 750 days) with Saudi patients presenting significantly later than non-Saudis (148.2 days vs 71.1 days; p=0.0044). The cervical groups of lymph nodes were the most commonly affected being the only site of involvement in 70 (51.9%) patients. Table 2 gives the distribution of the sites involved. One hundred and sixteen patients (85.93%) had localized lymphadenopathy defined as involvement of one group of nodes in eight of whom the involvement was bilateral. Twelve (S.89%) patients had limited lymphadenopathy defined as involvement of 2to 3 groups of lymph nodes while 8(5.93%) had generalized lymphadenopathy defined as involvement of more than three groups of lymph nodes. organomegaly in the form of hepatomegaly, splenomegaly or both occurred in 43(31.2%) patients. These were either clinical or sonographic findings. Erythrocyte sedimentation rate was normal in 18(13.33%) patients. In the remaining patients, it was abnormal. The values ranged between 1 and 145 with a mean of 56 (SD = 33.59). TST test was considered as positive if there was an in duration of more than 10mm. It was positive in 122(90.3%) patients. A definitive diagnosis was possible from FNA either by demonstration of acid-fast bacilli or caseating granuloma in 29 of 71(36.7%) patients who had this test. Acid-fast bacilli were identified either by culture of FNA or biopsy material in 40(29.6%) patients. In all the other specimens, diagnosis was reached on histology of excised lymph nodes. None of the 50(37%) patients tested for the human immunodeficiency virus was positive for the virus. This included all patients with organomegaly and/ or generalized lymphadenopathy. At follow up all patients recorded an increase in weight ranging from 3 kilograms to 15 kilograms with a mean of 5.6kilograms. Ten (7.4%) patients noted an increase in size of the lymph nodes, which was clinically documented. In one patient there was sinus formation necessitating incision and drainage. Steroids were used in4 of the patients with resolution of lymphadenopathy. In 5(3.7%) of patients the transaminases were elevated above five-fold the upper limit of normal. One of these patients had earlier anti-tuberculous medications for a week and stopped. In all patients re-introduction of the same first line therapy was tolerated. Treatment was extended to 9 months in these 15 patients who either had paradoxical reaction or hepatitis .In 46(34.1%) of patients there was residual lymphadenopathy at the time of completion of therapy. All patients recorded increase in weight and resolution of symptoms.

Table - 1. Frequency of Symptoms

	Number	Percentage
Swelling + Discharge	107	79.3%
Fever	46	34.1%
Pain	34	25.2%
Night Sweats	21	15.6%
Weight loss	18	13.5%
Cough	13	9.6%
Others	16	11.9%

Discussion:

Tuberculous lymphadenopathy (TBLA) remains the commonest cause of lymphadenopathy as well as the commonest cause of extrapulmonary tuberculosis in most developing and transition countries. This study demonstrated that TBLA in adults in Saudi Arabia is principally a disease of the young with over 54% of the patients being under the age of 35 years. This is compatible with the findings in the developing world. In the western world though, it tends to be a disease of the old. A recent study from Germany for example revealed the population to be older at 40.9 years but, like this study, the natives were significantly older than the immigrants/expatriates (53.8 years vs 35.5 years) [8]. There is a clear female preponderance with over three females to one male. Female preponderance has been observed in TBLA in similar studies from this region as well as elsewhere [5,8]. The high number of female domestic servants from Indonesia and the Indian subcontinent in this study may partly explain this RMC being the only hospital freely accessible to them. Thus for every one non-Saudi male patient, there were five non-Saudi female patients compared to a figure of.1:2 among the Saudi patients. Another explanation is probably the higher chance of transmission of tuberculosis in females in communities where they are sequestrated in enclosed areas for prolonged periods of time. As observed in the western world, the immigrant population in Saudi Arabia tends to constitute a high proportion of cases (over 54%). Of this number, the Indonesians make up the majority. This may be related to the fact that a majority are domestic servants and from a poor background and therefore more prone to tuberculosis as well as being confined to the home. Narang et al in a study of nearly 8,000 children showed that prevalence was 34 times higher in children with positive family history of tuberculosis than in those without a history and that there was an association between prevalence and the living standards of the children, with a higher prevalence in families that belonged to an underprivileged social class living in thatched, improvised houses[9]. A study of extrathoracic tuberculosis in HIV - negative adults in the United States also identified the disease to occur more frequently in females and in immigrants from countries other than the Americas - persons from India, South-east Asia and the Eastern Mediterranean [10]. Africans comprise d 71% of cases of TBLA in a Danish University Hospital [11]. The relative paucity of this condition among patients from Africa and other Arab nations in this study is, however, difficult to explain.

Presentation, in our population seems to be late especially among the Saudi patients with a median duration of 60 days. This however is much earlier than the reported duration of over L year in 43.75% of patients from India [12]. In a study by Hochedez et al from France, HIV positive patients presented much later than HIV negative patients (2 months vs. 1 month)[13]. Although a majority presented only with local symptoms, constitutional symptoms occurred in more than a third of the patients. This is similar to the figure reported by Memish et al (n in whom there was only one patient who was HIV positive. Geldmacher et al [8], however reported that all their patients had constitutional symptoms although only one was HIV positive. Our findings therefore support the view that symptomatology Per se does not indicate the presence of co-infection with the HIV making it a nondiscriminatory factor in differentiating between HIV positive and negative patients. Although only 13.3% of the patients gave history of weight loss, all patients gained weight of at least 3 kilograms while on treatment. It is obvious therefore that most of the patients had an insidious disease course that was not noticeable by them. Weight loss is therefore a very common feature of tuberculous lymphadenopathy even in HIV negative

populations. As in most other studies of TBLA, the cervical group of lymph nodes is the most commonly involved. This may be explained by the fact that the bacilli deposited in the pharynx and tonsils spread by lymphatics to the cervical group of nodes. Deposition of the bacilli in the lungs will also put the mediastinal

Table - 2. Distribution of Lymphadenopathy According to site

	Number	%
Localized	75	55.56
Cervical	13	9.63
Supraclavicular	9	6.67
Axillary	5	3.70
Inguinal	5	3.70
Submandibula	5	3.70
Intrathoracic	1	0.74
Intra abdominal	**14**	**10.37**
Limited	**8**	**5.93**
Generalized	**135**	**100.00%**
Total		

group of lymph nodes as the primary site of drainage. In this study, where a chest radiograph was done in all patients, there was isolated thoracic involvement in only 5(3.7%) of patients. This makes the haematogenous spread to the cervical nodes as a less plausible explanation for the predominance of this group in TBLA. Twenty (14.8%) patients had involvement of more than one group of lymph nodes and in 8(5.9%) it was generalized making this clinical finding also non-discriminatory between HIV positive and negative patients. This study therefore supports an earlier study that showed clinical findings in TBLA to be similar between HIV seronegative and positive patients [14].

The finding of lymphadenopathy often leads to a series of diagnostic tests with a view to ultimately reaching a tissue diagnosis. The identification of acid fast bacilli (AFB) by culture or microscopy or the presence of caseating granuloma in the right clinical setting is largely taken as diagnostic of TBLA. Tissue is best and more easily obtained by fine needle aspiration (FNA) for histology and culture. In this study the yield from this method was poor at 36.7%. This is partly because mycobacterial culture was not requested in all the cases that had non-conclusive results and subsequently underwent excisional biopsy. Other studies have however shown FNA to have a high sensitivity and specificity. Jha et al had a positive result in 52 out of 56 patients (92.9%) while Chao et al reported a sensitivity of 88% and a specificity of 96 % [15,6]. The isolation of acid-fast bacilli from the FNA material is higher in purulent aspirates, followed by caseous and least often in blood-mixed particles [17, 18]. Granulomas were most often seen when the aspirate was blood-mixed particles, followed by caseous and, least often, pus [17]. Tuberculin skin testing has been used as a basic tool for the diagnosis of tuberculous injection and its combination with FNA has been shown to increase the sensitivity to 90% [19]. To obviate the need for excisional biopsy, therefore multiple punctures should be undertaken adequate material obtained for both cytology and culture and the result correlated with the TST. Culture of FNA or biopsy material was requested in less than one third of the patients in this study. In a large series of 1838 patients with TBLA by Ehring, culture was positive in only 18 %[20]. That not withstanding, the increasing resistance of M. tuberculosis to first line anti-tuberculous drugs makes it prudent to request for culture and sensitivity in all lymph nodes specimens. It is the policy however in some countries not to routinely culture specimens of lymph nodes for AFB [21]. Mycobacterium tuberculosis polymerase chain reaction (PCR) for mycobacterial DNA sequences on the FNA or biopsy specimens has been shown to have a sensitivity, specificity, positive predictive value, and negative predictive values of 43.33,100, 100, 63.83 per cent respectively [21]. It is an expensive test thus making it suitable for confirmation in difficult cases rather than for screening. None of our cases had this done during the period under study.

All our patients received the WHO Category I treatment schedule except for 15 patients who had treatment related hepatitis or paradoxical reaction. Although all our patients showed clinical improvement and objectively gained weight, a significant number of patients had residual nodal enlargement. Furthermore, the follow up period was too short to exclude relapse. In meta-analysis of 8 six-month and 3 nine-month schedules, van Loenhout-Rooyackers et al reported relapse rates of 3'3% and 2.7% respectively [22] concluding that six -month regimes are adequate for the treatment of TBLA. Except for instances where excisional biopsy is performed for diagnostic purposes, surgery is not indicated in the management of TBLA due to M. tuberculosis.

Paradoxical deterioration during antituberculosis therapy, defined as the clinical or radiological worsening of pre-existing tuberculous lesions or the development of new lesions in a patient who initially improves, may be confused with bacteriological relapse. The incidence may be as high as 23% in lymph node tuberculosis [23]. It represents a hypersensitivity to tuberculoprotein and a surge in the lymphocyte count, accompanied by an exaggerated tuberculin skin reaction, was observed in some patients with this reaction [24]. The reported co-existence of TBLA with malignancies [25, 26, and 27] should make this diagnosis one of exclusion.

In conclusion, TBLA lymphadenitis in Saudi Arabia is more common among females and the expatriate population. Clinical features are similar to other areas and not at variance with those reported from areas with high HIV-prevalence Culture of biopsy material is under utilized. Response to therapy with standard drugs is good.

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Evaluation of a Doppler Echocardiographic Index Of Global Ventricular Fundtion In Dilated Cardiomyopathy

Sohaib Ahmad,MD; M.U. Rabbani, MD,DM; Nadia Shirazi, MD

Abstract

Diastolic and systolic functional impairment co-exists in patients of dilated cardiomyopathy (DCM). The indices of systolic function like left ventricular ejection fraction (LVEF) and fractional shortening have been utilized over years as a measure of the left ventricular function but ejection fraction may be erroneously calculated in patients with mitral and aortic regurgitation, very commonly associated with heart failure in DCM. Also, the LVEF does not correlate with the angiographically estimated value. Diastolic function indices correlate well with the functional status (NYHA) but presence of mitral regurgitation and atrial fibrillation does not permit an accurate assessment in such patients.

Our study aimed at correlating the clinical status (NYHA class) of patients with DCM with heart failure, at the time of presentation, with the systolic (LVEF, left ventricular end-diastolic diameter) and diastolic indices (E- and A- deceleration time) individually and with the Tei index (index of myocardial performance) that combines the systolic and diastolic parameters and is independent of the heart rate and mitral regurgitation.

An analysis of 60 such patients revealed that a successive shortening of E- and A- deceleration time and increased value of Tei index correlated significantly with the clinical status and proved to be more informative than the systolic function indices.

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Impairment of left ventricular contractile function is the major abnormality in dilated cardiomyopathy (DCM) and is usually associated with chamber enlargement. Patients with dilated cardiomyopathy often have impairment in contractile reserve, which produces a reduction in fractional shortening with modest increments in end-diastolic diameters. Dilated cardiomyopathy, often considered as a condition of left ventricular (LV) systolic dysfunction, encompasses diastolic dysfunction in addition to systolic functional impairment and studies have demonstrated the coexistence of systolic and diastolic dysfunction in majority of patients with congestive heart failure [1] Diastolic dysfunction is the initial alteration in dilated cardiomyopathy and studies have demonstrated the presence of impairment of left ventricular relaxation as well as abnormalities of LV compliance in patients with dilated cardiomyopathy [2].

Systolic and diastolic time intervals are closely linked to systolic and diastolic left ventricular performance[3,4]. Systolic time intervals have been found to be correlated closely with cardiac output, ejection fraction and the first derivative of isovolumic left ventricular pressure in patients with and without cardiac disease [3,5] The pattern of the early and late diastolic mitral inflow velocity as well as duration of the isovolumic relaxation time, reflect diastolic left ventricular performance [4,6]

However, an accurate assessment of diastolic dysfunction is difficult especially in the presence of advanced symptomatology, tachycardia, mitral regurgitation and abnormalities of ventricular distensibility and relaxation. Although, several studies have revealed a higher correlation between clinical status and echocardiographic parameters reflecting entirely diastolic dysfunction, left ventricular ejection fraction (LVEF) is the most commonly utilized parameter for the assessment of LV functions.

Overcoming many limitations, the index of myocardial performance was devised in 1995, which combines the diastolic and systolic parameters and shows no significant influence of heart rate or of mitral regurgitation often present in patients with congestive heart failure [7]. It is easily obtained and may be used in the workup of patients with suspected cardiac dysfunction [1]

Objectives

The present study was conducted to assess the correlation between the clinical status (NYHA class) of patients with dilated cardiomyopathy to systolic and

Key words: Tei index, Diastolic function, Dilated Cardiomyopathy, Doppler echocardiography, Index of myocardial performance

diastolic parameters individually and to Tei index which combines both systolic and diastolic performance and to compare their accuracy in highlighting the left ventricular dysfunction and clinical status individually.

Methods

A total of 60 patients with echocardiographically proven dilated cardiomyopathy with symptomatic heart failure were assessed clinically and classified according to their clinical status into three groups – group 1: NYHA class II (n=13); group 2: NYHA class III (n=23); and group 3: NYHA class IV (n=24). None of the selected patients demonstrated atrial fibrillation, atrio-ventricular block, valvular or pericardial disease.

All the patients were subjected to a detailed color-Doppler echocardiographic examination according to the recommendations of the American Society of Echocardiography [1] using the commercially available ATL-HDI 1500 ultrasound system. The left ventricular dimensions were measured at the mid-ventricular level using M-mode in the parasternal long-axis view. Left ventricular ejection fraction (LVEF) was calculated using Simpson's method in the apical view. The analysis of mitral inflow velocity by pulsed-wave Doppler echocardiography in the apical four-chamber view was used for assessment of diastolic function and for each parameter, three consecutive beats were measured. Velocities in early [E] and late diastole [A] were measured, and deceleration time was defined as the time from the E- or A- peak intersection with the baseline. Deceleration time was not assessed if E and A were summated as in tachycardia. Systolic/diastolic performance (Isovolumetric contraction time [ICT] + Isovolumetric relaxation time [IRT]/ Ejection time [ET]) was calculated following analysis of Doppler time intervals as described by Tei et al [7].

Statistical Analysis

Continuous data are expressed as mean ± standard deviation (SD); the differences in category variables were analysed by chi-square analysis and differences in continuous variables by Wilcoxon Signed Ranks test. Probability values < 0.05 were significant.

Results

Among the patients' characteristics at baseline, heart rate was significantly higher and blood pressure lower (systolic as well as diastolic) in NYHA classes III and IV than in class II and the severity of mitral regurgitation significantly greater in high NYHA classes. However, the incidence of mitral regurgitation and differences heart rate did not vary significantly among the impending NYHA classes.

Figures 1 - 5 demonstrate the cardiac status (NYHA class) in relation to LVEF, E- and A- deceleration time and Tei index. LVEDd (Left ventricular end-diastolic dimension) values (Figure1) and echocardiographically estimated LVEF showed no correlation to the severity of cardiac disability in patients with congestive heart failure (Figure 2). ($p > 0.05$)

The Doppler time intervals (E- and A- deceleration time) were significantly shorter with increasing NYHA class (Figures 3 and 4). The systolic/diastolic performance [ICT + IRT/ ET] was significantly greater with increasing NYHA class (Figure 5). Hence, the diastolic and combined systolic/ diastolic parameters correlate with progressively declining LV function ($p < 0.05$).

Discussion

Left-ventricular ejection fraction has consistently proven to be good indicator of cardiovascular function; however, it relies on various ventricular factors such as left ventricular geometry, or is based on erroneous assessment of ventricular contractility in patients with aortic or mitral regurgitation, most of the patients presenting with congestive heart failure. Additional reliable information on ejection fraction depends significantly on satisfactory echo conditions. This may represent the widely dispersed LV-EF findings in our study that showed no correlation to NYHA classes and only poorly reflected the clinical status of patients with congestive heart failure.

A variety of diastolic abnormalities have been described in patients with dilated cardiomyopathy; one of the most useful and reliable signs is the abnormal closure of the mitral valve, which reflects a late diastolic equalization in transmitral pressures. Pulsed-wave Doppler interrogation of mitral flow velocity shows a spectrum of diastolic abnormalities in dilated cardiomyopathy. Different studies have demonstrated the presence of both impairment of left ventricular relaxation and abnormalities in compliance in such patients. It is important to emphasize that left ventricular diastolic function reflects a complex interaction of left ventricular relaxation, chamber stiffness, loading conditions and temporal or spatial non-uniformity in ventricular function. All these factors and others such as age, heart rate and the coexistence of mitral regurgitation should be considered while evaluating LV diastolic function. In our study, the successive shortening of E- and A- deceleration times owing to increasing LV filling pressures correlated significantly with NYHA grades and the process of declining LV function. These observations were similar to the findings of Dahm et al [2], Tennenbaum et al [6] and Fruhwald et al [7].

Several investigators have confirmed that severe diastolic dysfunction may be overlooked in heart failure patients with elevated filling pressures due to pseudo-normalization of the mitral inflow [4,10,11,12]. Therefore, in addition to conventional Doppler-derived parameters, other methods such as tissue Doppler imaging or analysis of the mitral inflow flow propagation velocity are being increasingly used to identify these patients [13,14].

Tei index that combines both systolic as well as the diastolic performance reflects "global" LV-function better than the isolated evaluation of either ejection or relaxation. Studies have shown that isovolumetric contraction [ICT] and isovolumetric relaxation time [IRT] accurately reflect systolic and diastolic function [15,16]. Initially, prolonged LV relaxation is associated with increased isovolumetric relaxation time; with worsening LV dysfunction factors like left atrial pressure and mitral regurgitation also influence the relaxation time. Progressive lengthening of the sum of isovolumetric relaxation time and isovolumetric contraction time compensates for the variable change in isovolumetric relaxation time as the LV dysfunction continuously worsens, thus rendering the Tei index independent of the changes in individual components [2,7].

Dujardin et al demonstrated that higher values of Tei index in patients of heart failure than in healthy individuals were attributable to prolongation of isovolumic contraction time and a shortening of ejection time; also Tei index was significantly correlated with NYHA class, ejection fraction and ventricular volumes and values > 0.77 with higher 1-, 3- and 5-year mortality [17]. Sutton and Weigers [18], and Harjai et al [19] put similar forth results from their studies. In our study increasing values of Tei index was associated with an advanced NYHA class, restrictive filling pattern but no significant correlation with LVEF.

Parthenakis et al concluded from their study that a high value of Tei index was associated with advanced NYHA class and a restrictive filling pattern while a negative correlation existed between Tei index and systolic indices (stroke volume, cardiac output), diastolic indices (E/A, A) and cardiopulmonary exercise testing parameters (peak oxygen consumption, anaerobic threshold) [20].

The results show that Tei index in combination with the systolic and diastolic function indices provides a more or less accurate assessment of the clinical status and hence may be used as a non-invasive predictor of morbidity and quality of life and with further evaluation may emerge as a predictor of mortality in patients of heart failure.

Conclusions

The determination of diastolic function of left ventricle determined by Doppler echocardiography and the combined systolic / diastolic performance index (Tei index) in patients with

dilated cardiomyopathy enables a reliable determination of LV function and should be utilized routinely in addition to systolic function for the determination of prognosis and correlation with the clinical status, as the values of LVEF determined echocardiographically have no or little significant correlation with the same.

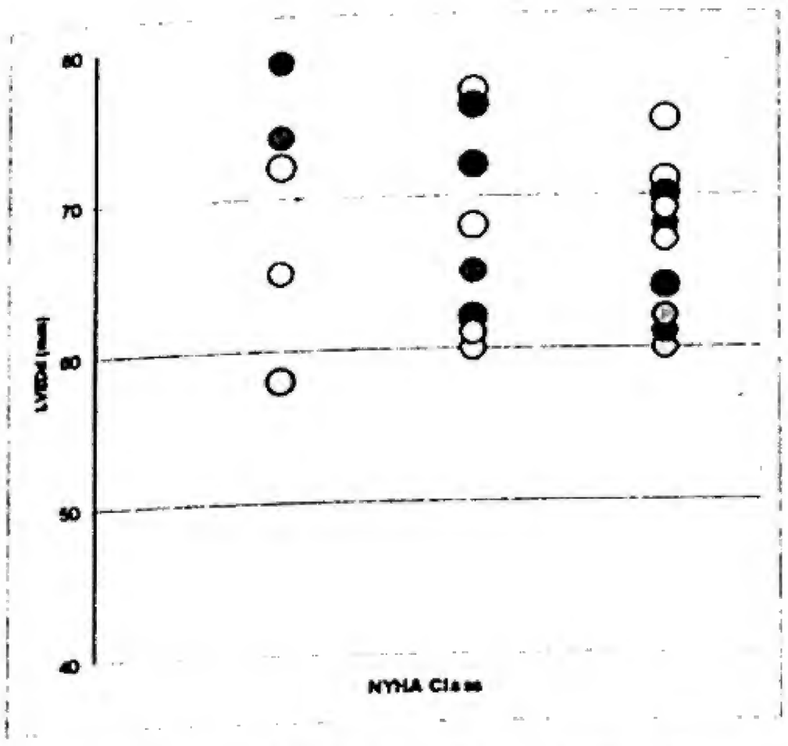

Figure 1: Left ventricular end-diastolic diameter (LVEDd) measurements obtained by echocardiography of the 60 patients in different NYHA classes

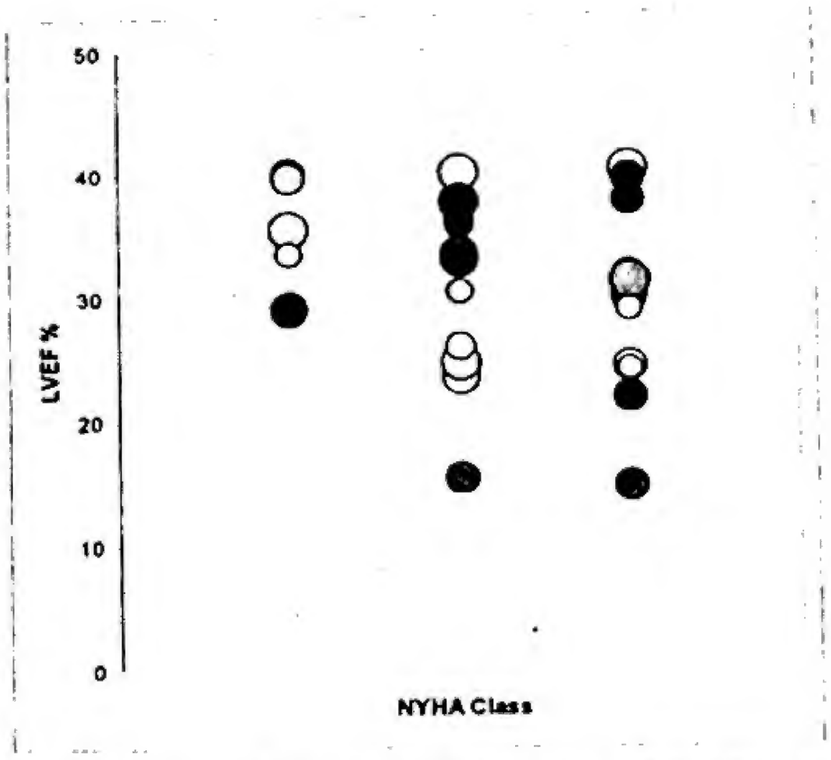

Figure 2: Left ventricular ejection fraction (LVEF) obtained by echocardiography of the 60 patients in the different NYHA classes

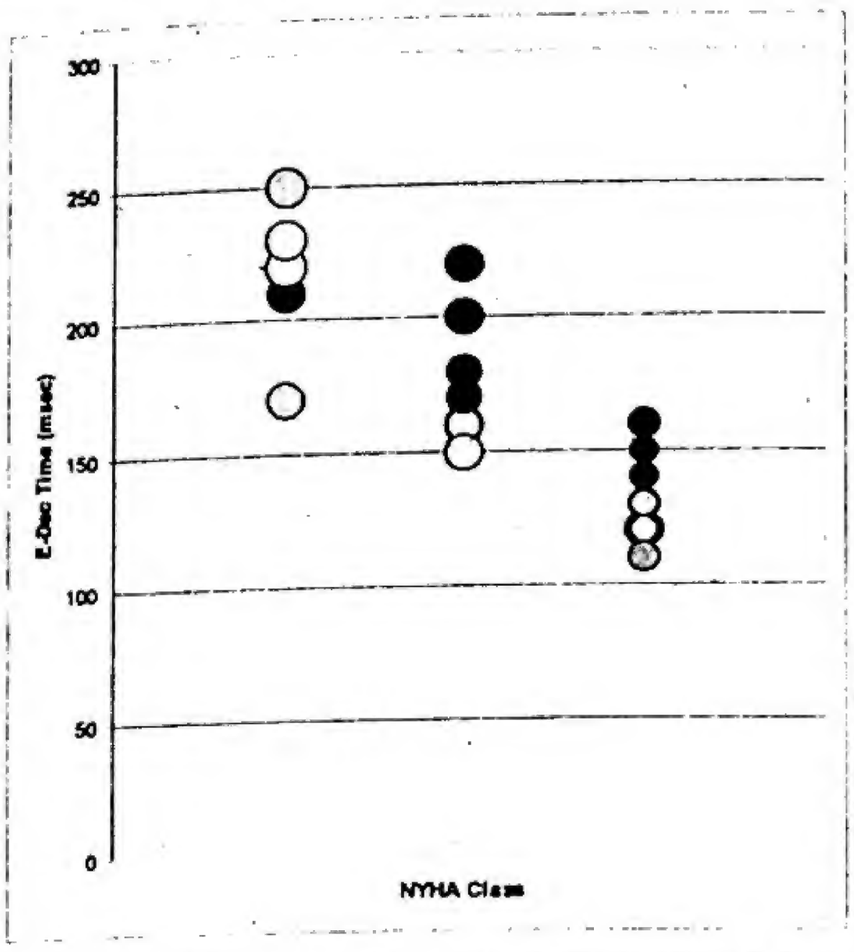

Figure 3: E-deceleration time of the 60 patients in the different NYHA classes

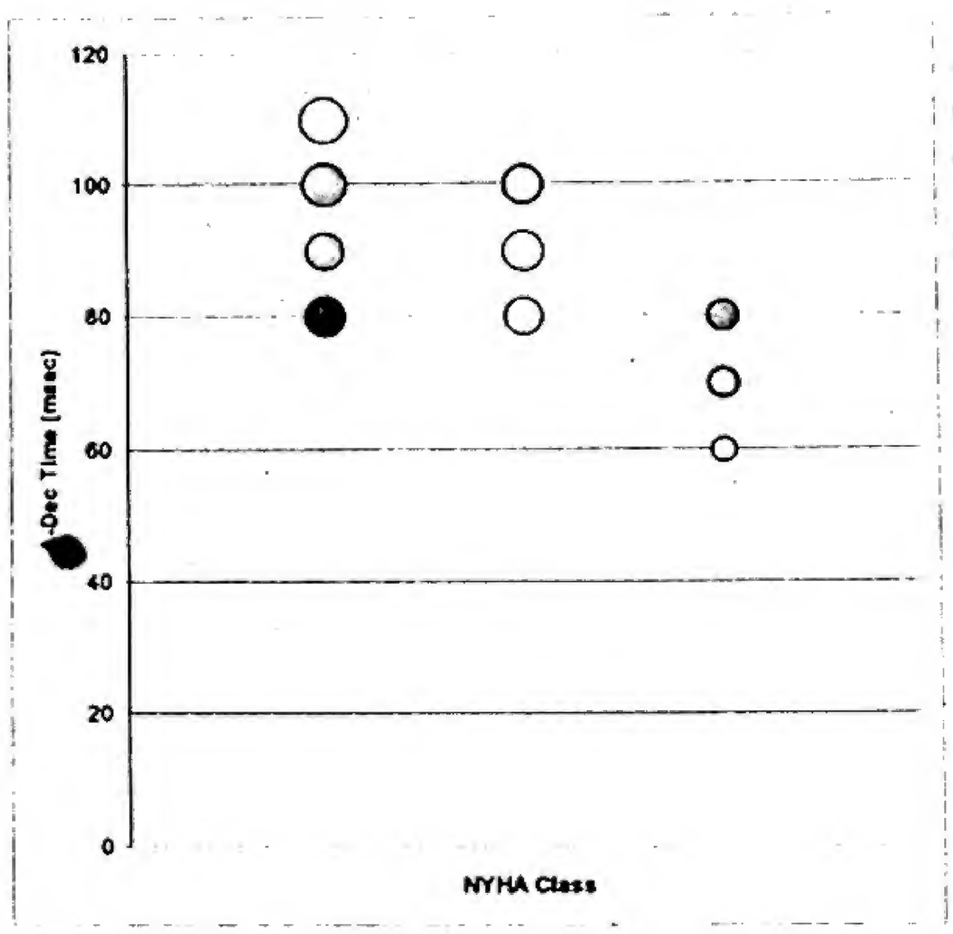

Figure 4: A-deceleration time of the 60 patients in the different NYHA classes

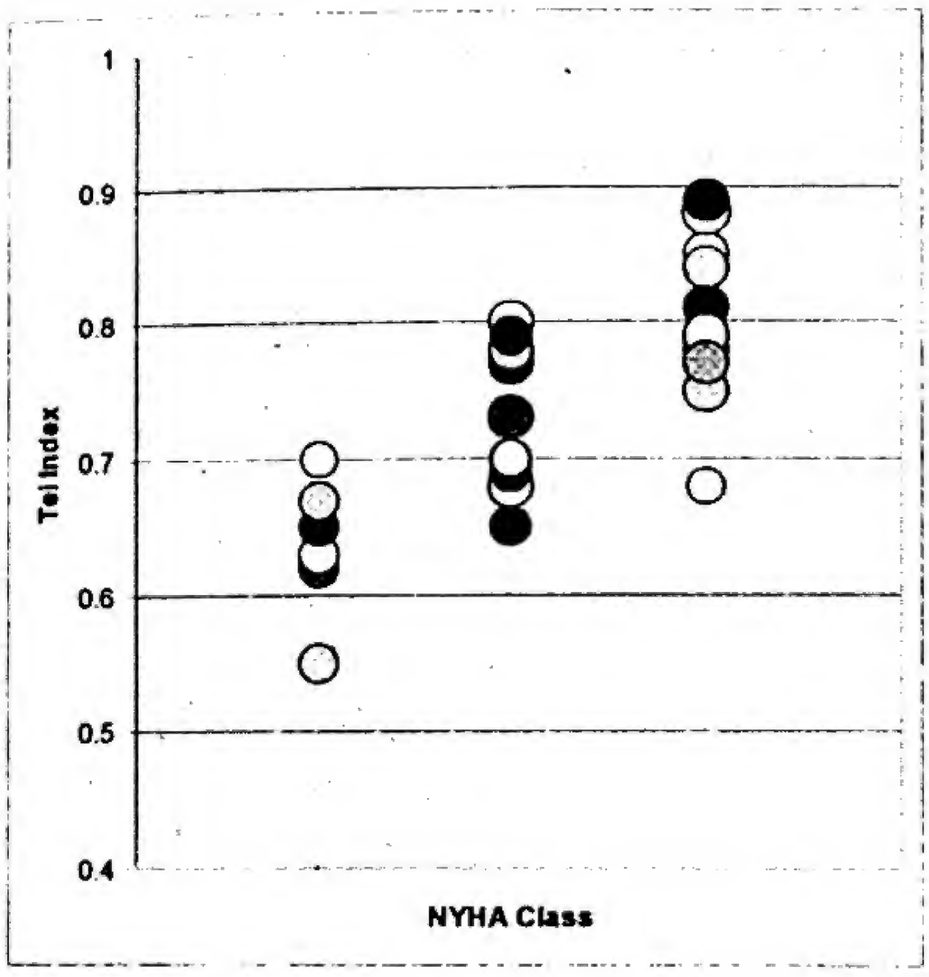

Figure 5: The systolic/ diastolic performanc e (Tei index) of the 60 patients in the different NYHA classes

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Role of Intrapleural Streptokinase in Management of Multiloculated thoracic empyemas

Naveed Nazir Shah, Arshad Altaf Bachh, Rakesh Bhargava, Zuber Ahmad, D.K. Panday, Mohd. Shameem

Abstract

Multiloculated thoracic empyemas which are incompletely drained by tube thoracostomy alone usually require surgical intervention. Non surgical approach with the use of a fibrinolytic agent like streptokinase is an effective alternative modality which can avoid a thoracotomy .To evaluate the utility of streptokinase in the management of multiloculated empyemas, a single blind randomized case control study was conducted.36 cases of multiloculated thoracic empyemas were included with failure to drain less than 100 ml/24 hrs through tube thoracostomy. Cases were randomized into two groups as 18 cases of streptokinase group and 18 cases of control group. Streptokinase, 2.5 MU in 100 ml 0.9% saline solution was instilled daily into the chest tube for 6 consecutive days. In control group, 100 ml of normal saline was instilled intrapleurally through intercostal drain. Assessment was done on the basis of clinical improvement, amount of drainage, duration of chest tube in situ and radiological improvement by chest x-ray .The study revealed clinical improvement, increased drainage through chest tube, shorter duration of intercostal drainage in situ and radiological improvement in the streptokinase group compared to control group. The observation difference is found to be highly significant statistically. No major adverse effects were noted in streptokinase group.The study concludes the safety, efficacy, reduced hospital stay and decreased morbidity in patients of loculated empyemas in whom streptokinase was instilled intrapleurally as compared to control group.

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INTRODUCTION:

Empyema is a collection of pus in a natural cavity. A pleural empyema is defined as pus in the pleural space. Drainage of pleural empyema by making an opening in the chest was first described by Hippocrates[1]. Modern day management by closed drainage which has resulted in a dramatic fall in mortality as based on the principles developed by Evarts Graham and the World War I Empyema Commission[2].

Some patients fail to recover with simple drainage inspite of intercostal tube insertion and aggressive antibiotic therapy. Most of these have progression of the acute empyema to the fibrinoplurent stage with multiple loculations and viscous pus[3]. These patients are managed by surgical intervention, early thoracotomy and decortication being currently preferred modalities[4].

Streptokinase was developed in 1944, the first clinical application of this drug was by Tillet & Sherry in 1949 for intrapleural instillation in cases of acute fibrinous pleurisy, bacterial empyema and haemothorax.[5] Since then many others have reported on the utility of intrapleural streptokinase in facilitating empyema drainage by a chest tube, avoiding a major thoracotomy[6-18]

The present study was undertaken to evaluate the utility of streptokinase in empyema which acts by dissolving the septations in pleural space and hence preventing development of restrictive lung disease.

MATERIALAND METHODS:

Thirty six patients with multiloculated empyema were studied at Department of TB & Chest Diseases, Jawaharlal Nehru Medical College and Hospital, AMU, Aligarh, U.P. from Feb. 2004 to August 2005.

Cases were randomized into two groups:

Group-A: Streptokinase group: 18 cases
Group-B: Control group: 18 cases

Patients were diagnosed on pleural fluid analysis including Gram staining, ZN staining and culture. All the patients had standard postero-anterior and lateral chest radiograms. USG thorax was performed on all patients before therapy and many had follow up USG upon completion of therapy. Additional CT scan thorax was carried out in 6 cases.

The decision to insert chest tube followed the recommendations of Light[12]

Inclusion Criteria:

Stage I acute exudative or stage II fibrinopurulent empyemas, were included

Key words: Empyema, Streptokinase, Thoracostomy

(as defined by subcommittee on surgery of the American Thoracic Society[19].

Other Criteria:

(1) Exudative pleural fluid as described by Light[20].

(2) Pleural fluid with at least one of the following:
- pH < 7.20
- Glucose < 40 mg/dl
- LDH > 1000 IU/L
- Total protein > 5 g/dl /grossly purulent appearance
- WBC count > 20,000/dl
- Positive Gram stain or growth on culture

(3) Clinical toxicity with fever or leucocytosis

(4) Multiloculations of fluid as demonstrated on USG thorax.

(5) Failure or less than 1000 ml/24 hrs drainage in tube thoracostomy without radiological or clinical improvement.

The etiology of empyema was presumed to be pneumonic or tuberculous.

The diagnosis of tuberculous empyema was made using the following criteria.

(1) Family history of tuberculosis

(2) Biochemical criteria of exudative pleural effusion as described by Light.

(3) Sputum or pleural fluid analysis for acid fast bacilli.

(4) Associated lung parenchymal lesions consistent with radiological diagnosis of tuberculosis.

(5) Negative routine bacteriological smear and culture.

Exclusion Criteria:

Patients excluded were those with

(1) recent major surgical procedure

(2) long standing chronic draining empyema[13] with a bronchopleural fistula

(3) stage III chronic organizing empyema with a thick pleural peel as demonstrated by USG thorax.

Streptokinase instillation:

Patients were placed in lateral decubitus position with the unaffected lung dependent, and streptokinase 2.5 MU in 100 ml of 0.9% saline solution was instilled intrapleurally. Tube was clamped and the patient was rotated in various positions and clamp released after 4-6 hours. The procedure was repeated daily for 6 consecutive days[12]. In control group, 100 ml of normal saline was instilled intrapleurally for 6 consecutive days through intercostal drain.

Assessment of Response:

The patients were assessed for a favourable response as demonstrated by –

(1) Resolution of fever and systemic and respiratory symptoms.

(2) Increased chest tube drainage

(3) Decreased duration of intercostal drainage in situ.

(4) Evidence of radiological improvement by standard chest radiogram and/or USG thorax.

X-rays were taken 24 hrs before instillation of streptokinase and were repeated after the complete course of therapy on 7th to 10th day and thereafter whenever required. Cases were followed up for a minimum period of 8 weeks. In order to score the changes in chest x-ray, dimensions to pleural effusion were estimated by measuring two maximal diameters at right angles to each other.

Radiological arbitrary scoring system was used as described by Bouros et al[12] as follows:

0 - No change
1 - Less than 1/3rd improvement
2 - Improvement between 1/3rd and 2/3rd
3 - More than 2/3rd improvement

Volume of pleural fluid drained from chest tube was recorded daily. Any adverse effect to drug streptokinase like fever, pain, allergic reactions or haemodynamic changes, bleeding was observed. Fever was defined as temperature greater than 38 C, or one degree elevation over baseline in previously febrile patients. The chest tube was removed when total quantity of fluid through chest tube measured less than 50 ml in 24 hrs.

Control study was taken with similar aetiopathological cases and treated par with streptokinase group.

OBSERVATIONS AND RESULTS:

The study and control group consisted of 18 patients in each. The age ranged from 15-70 years in both the groups. Both the groups had 12 males and 6 females. Of the 18 patients in each group, 6 were non tubercular who received antibiotics according to culture sensitivity report, while 12 were tubercular who received standard antitubercular regimen (2HRZE/4HR). Of the 12 patients in study group 4 cases were having fluid AFB positivity while AFB was positive in 3 cases in control group.

All the 18 patients in streptokinase group remained well and did not need further surgical intervention. The volume of pleural fluid drained following streptokinase instillation (after subtracting 100ml) ranged from 1300 to 2300 with mean of 1804.44 ±542.94 in 6 days. Streptokinase was tolerated by all the patients. The chest tube drainage in the control group ranged from 170ml to 500 ml (Mean 269.44 ± 179.73).

The observation revealed that there was significantly higher volume of fluid drained in study group A as compared to group B (SE of difference = 67.4, RD = 22.77)(Table 1).

Table 1:
Comparative assessment of different variables of efficacy in streptokinase (A) and control group B.

	Parameters used	Group A (n=18)	Group B (n=18)	Test of significance
1.	Mean volume of fluid drained (ml)	1804.44	269.44	RD>2
2.	Mean duration of ICD in situ (day)	26.39	86.28	RD>2
3.	Mean radiological scoring	2.44	0.72	P<0.001

Statistical error of difference between two means is used to find out the statistical significance of amount of fluid drained and duration of ICTD in situ between streptokinase group and control group (RD > 2: statistically significant). Unpaired 't' test is used to find out the statistical significance of radiological scoring between streptokinase group and control group (P value < 0.05, statistically significant).

The duration of intercostals drain in situ after streptokinase instillation in group A ranged from 18 to 35 days with a mean of 26.39 ± 10.74 days whereas in control group the duration of intercostal drain in situ after placebo instillation ranged from 50 to 140 days with a mean of 86.28 ± 52.62 days. The difference in mean duration of intercostal drain in situ between the two groups was found to be significant statistically (RD > 2) (Table 1).

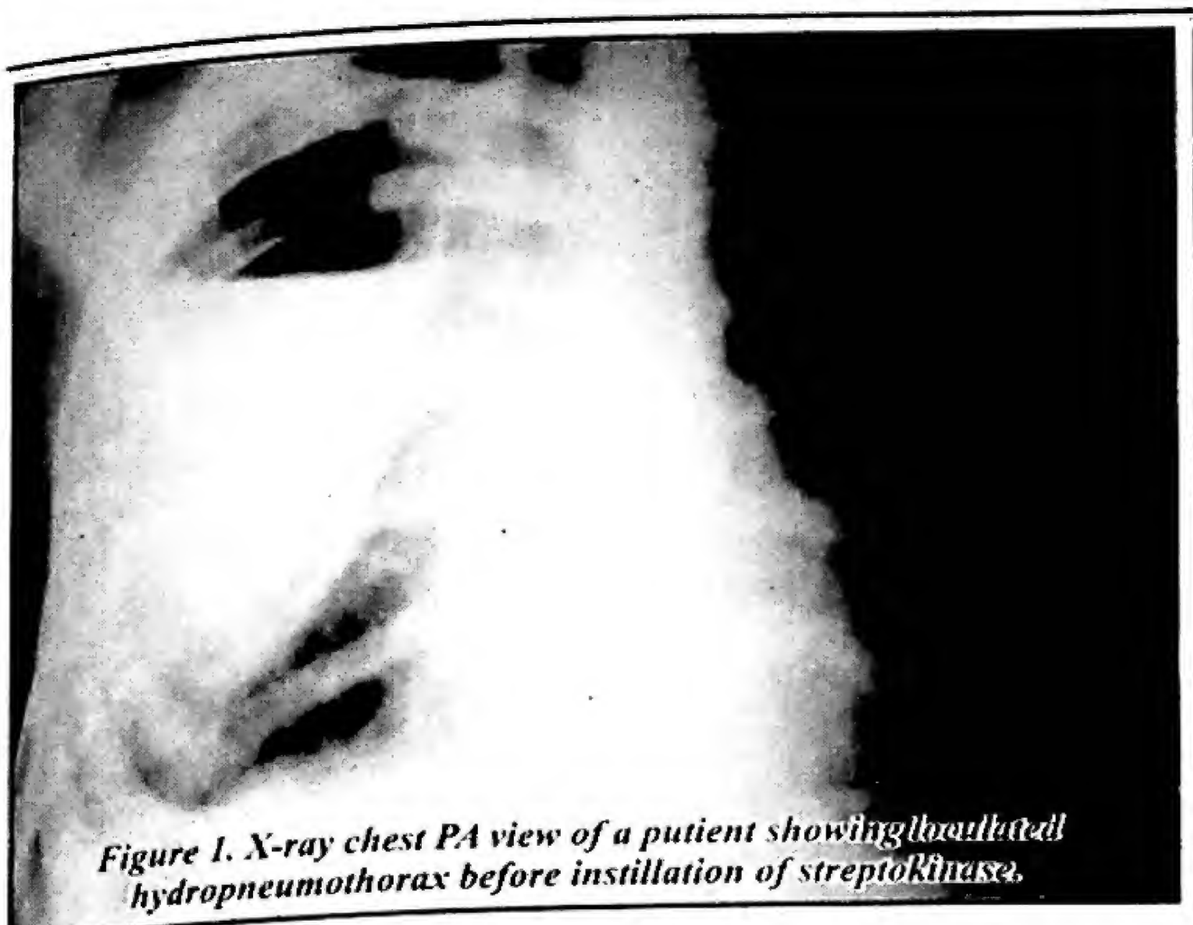

Figure 1. X-ray chest PA view of a putient showing loculated hydropneumothorax before instillation of streptokinase.

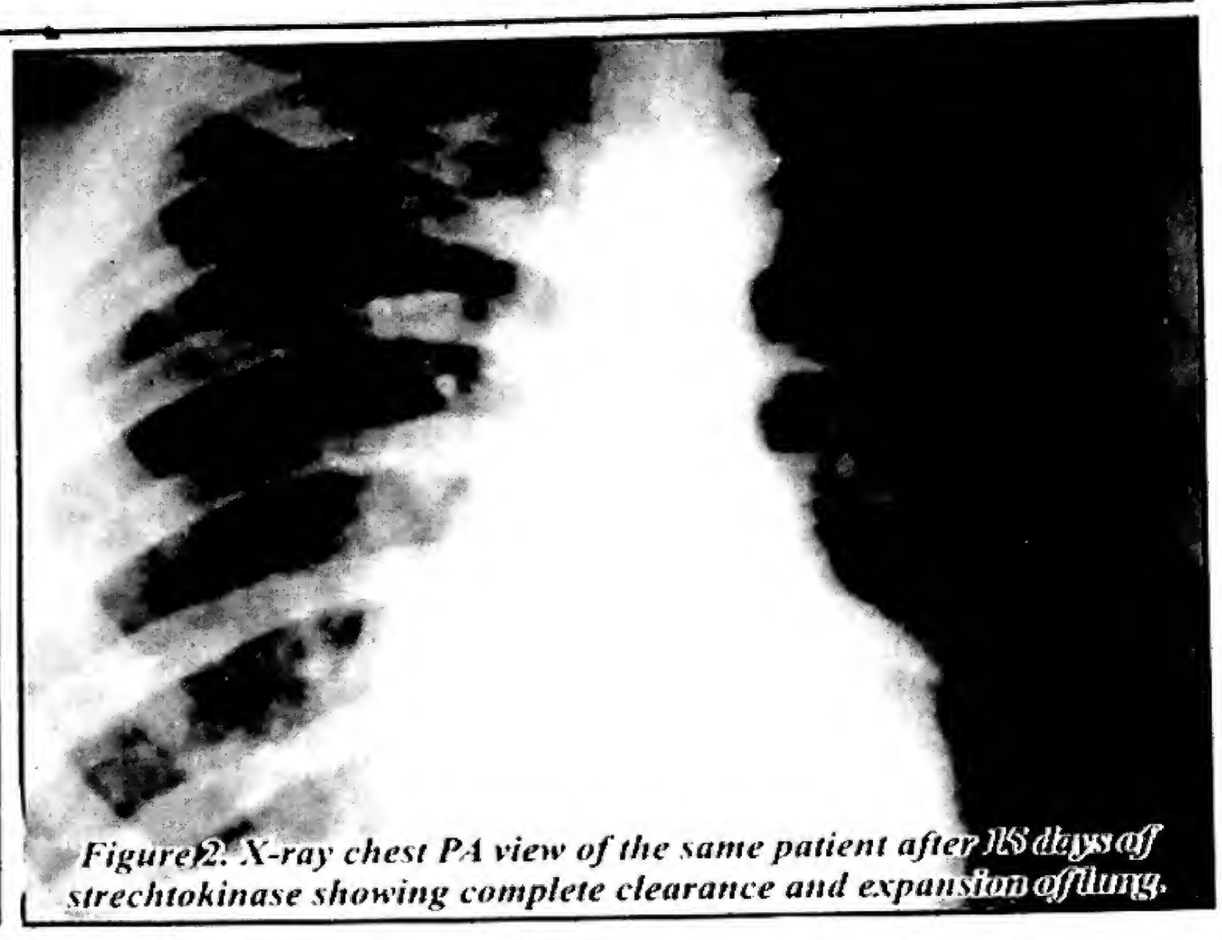

Figure 2. X-ray chest PA view of the same patient after 18 days of strechtokinase showing complete clearance and expansion of lung.

The radiological observations in streptokinase group revealed score 3 response improvement in 10 out of 18 cases (Fig.. 2) and score 2 improvement in 6 cases and score 1 in remaining 2 cases. While in the control group, score 2 improvement was seen in 3, score 1 improvement in 7, score 0 (no improvement) was seen in remaining 8 cases. The difference was found to be statistically highly significant ($P < 0.001$) (Table 1).

There were no adverse reactions to streptokinase therapy which would prompt to discontinue the therapy. Specifically there was no pain, dyspnea, any signs of new or enhanced bleeding, any signs of systemic absorption of fibrinolytic agent, or other indications of drug toxicity. Two patients developed sustained fever after 4th and 5th doses of streptokinase despite a clearing radiograph. In retrospect, it was thought to be an allergic reaction to streptokinase. Four patients complained of chest pain which was relieved by analgesics.

DISCUSSION:

Extension of infection of lung parenchyma (pneumonia) into the pleural cavity leads to pleural fluid accumulation, so called parapneumonic effusion. Contamination of this fluid leads to the development of an empyema. American Thoracic society in 1962 described 3 stages of an empyema. Stage I (the exudative stage) lasts for 24 hrs, has thin fluid with low cellular count; can be adequately treated with closed drainage with full expansion of lung. Stage II (the fibrinopurulent stage) is characterized by a thicker exudates, often with frank foul smelling pus containing polymorphonuclear leucocytes and fibrin with progressive tendency for loculation and development of a limiting membrane covering the visceral pleura preventing full lung expansion. This stage averages 7 to 10 days. In stage III (the organizing stage), fibroblasts grow into the exudate covering the visceral and parietal pleurae leading to formation of an inelastic pleural peel preventing lung expansion.

Stage I and some cases of stage II can be successfully managed by closed drainage while most stage II and III cases require surgical intervention.

Use of intrapleural fibrinolytic is another viable alternative to facilitate drainage and lung expansion in stage I & II empyemas inadequately treated by chest tube alone[5,6,18,19].

Streptokinase is a purified proteolytic enzyme derived from a bacterial protein of group C B hemolytic streptococci. Plasminogen is converted to a proteolytic enzyme plasmin by streptokinase. Plasmin then degrades fibrin clots and fibrenogen.

The present study was undertaken making use of this purified streptokinase in management of multiloculated empyemas when the drainage after intercostal tube drainage alone was inadequate. In our study radiological evaluation showed excellent results in 12 out of 18 cases (66%) moderate results in remaining 6 cases (33%). This is in accordance with the studies conducted previously[5,11,13-16]. Taylor et al in 1994[14] found complete resolution with re-expansion of underlying lung in 8 out of 12 patients (66.66%). Robinson et al in 1994[18] found similar success in 10 of 13 patients (77%). Sanchez et al in 1996[15] in their study had a success rate of 92% with complete resolution in 44%. Themes in 1996[16] in his study of 26 patients noted complete resolution in 16 out of 26 patients (62%), partial resolution in 2 out of 26 patients (8%).

In our study, dose of purified streptokinase used was 2.5 MU dissolved in 100 ml of Normal saline and the tube was clamped for 4-6 hrs. In practice the clamping period after streptokinase varied from 2 to 24 hrs [7,14,17]. Bergh et al[7] suggested a shorter instillation time of 4 hrs, combined with use of purified preparation contributed to reduced incidence of adverse effects.

No major adverse effects were noted in our study. The minor ones included fever and pleural pain[6,13]. Fever was perhaps due to a delayed hypersensitivity type reaction due to presence of some contaminating streptococcal proteins as well as from streptokinase itself rather than presence of a conventional bacterial pyrogen. Toxic responses like arthralgias, nausea, malaise and headache were also seen with earlier[21], although they appear to be less frequent with more purified preparations of this agent[10]. Anaphylaxis, which may occur in as many as 3.3% of intravascular administration of the agent[10] is very uncommon event with the intrapleural administration; reported in only 2 case reports till now[22]. Although the patients with bronchopleural fistula were excluded in our study, these type of patients have been treated successfully with streptokinase without any major adverse reaction.

CONCLUSION:

Multiloculated toxic empyema patients with incompletely drained pus have been managed by conventional open surgical approach which has resulted in substantial morbidity, mortality and expenses. Intrapleural fibrinolysis by streptokinase via-tube thoracostomy facilities complete pleural drainage and thus provides a safe, efficacious and cost effective modality of treatment. Subsequent surgical intervention is not jeopardized by prior use of streptokinase.

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Helicobacter pylori prevalence in Professional workers in main teaching Hospitals of Kashmir Valley.

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Abstract

The aim of this study was to compare the prevalence of H.pylori seropositivity among medical professional workers with that of general population. To determine whether different staff groups in an acute care hospital are at increased risk of acquiring H.pylori infection.One hundred fifty (150) medical professionals working in different departments and fifty (50) non professional persons of same age and sex were taken as controls. The serum was assayed for Ig G anti- H.pylori antibodies-The H.pylori positivity was 64% in professional workers and 48% in controls (P<0.05) H.pylori positivity had a positive correlation with age, being highest in the 20 – 35 years (57.47%). The seropositivity was higher in males in each age group as compared to females except age group 20 – 35 years was positivity was more for females (P>0.60). The H.pylori positivity rate in cases and controls were seen to differ significantly (P<0.05) in the female population while as in male population the difference was not significant (P>0.40). The H.pylori seropositivity was found in 72.10% of cases who were having gastrointestinal symptoms as compared to 47.82% of asymptomatic persons (P<0.01). The results showed an increasing positivity of H.pylori with increasing duration or work (P>0.20). The results showed a high H.pylori seropositivity in persons belonging to poor families (P<0.05). The prevalence of H.pylori was highest in professional workers. The seroprevalence of H.pylori positivity increased with increased age. The prevalence of H.pylori was more in males. The seroprevalence of H.pylori was more in poor families. The H.pylori infection was more in healthy workers with longer exposure to patients. H.pylori seropositivity was more in professionals with GI symptoms. H.pylori seropositivity was higher in Endoscopy staff dental surgeons and general surgeons as compared to rest of the theatre staff, nurse, medical students and sweepers.

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Introduction: - H.pylori was brought to worlds attention in 1983 when Warrwen and Marshall, two Australian investigators reported isolation of spiral organisms from mucosal biopsy specimens of patients with chronic active gastritis and peptic ulcer disease[1]. It is spiral shaped 0.5 X 3mm micro aerophilic gram negative rod with 4 – 6 sheathed multiple unipolar flagella with terminal bulbs. It resides below mucus layer in opposition to gastric epithelium in any location in which gastric epithelium is found, including the stomach and such metaplastic locations as the oesophagus, duodenum and Meckel's diverticulum[2]. H.pylori is one of the world's most common pathogens. The prevalence of organism is dependent on socioeconomic class, race and whether the subject resides in a developing country. The prevalence of infection increases with age in all populations and is significantly higher in the developing countries and is closely related to the low economic status. Japan is an exception among the developed Countries, the prevalence of H.pylori infection in people more than 40 years is approximately 80%. Overcrowding, suboptimal sanitary conditions, poor hygiene and low economic status are all factors thought relate to a high acquisition of H.pylori infection[3].

Increased seropositivity has been reported in endoscopists and nurses indicating an occupational risk[4]. H.pylori has been identified in drinking water using autoradiography chain reactions amplification[5].

H.pylori is spread largely by person to person contact, transmission via an external source such as water supply is a possibility but in general, infection is probably passed from person to person. Arguments for and against faecal-oral, oro-oral and gastro-oral transmission have been presented, but the dominance of these routes is still to be determined[3]. H.pylori infection has been incriminated to acute and chronic gastritis duodenitis, duodenal ulcer, gastric ulcer, non-ulcer dyspepsia, gastric adenocarcinoma gastric non-Hodgkins lymphoma of mucosa associated lymphoid tissue, coronary artery disease, rosacea, growth retardation in children[6]. H.pylori infection seems to be epidemiologically linked to the presence of cardiovascular and cerebovascular disease in diabetic patients[7], urtacarcia[8]. Multiple tests invasive and noninvasive are available for determining H.pylori infection. These are culture method, histological staining, direct

Key words: Helicobacter Pylori, Prevalence, Hospital

detection of urease activity, radioactive carbon urea breath test serological test. ELISA is the technique of choice for serological test because it offers the most versatility in regards to immunoglobulin specificity and relative ease of use. The sensitivity and specificity of the test is 97% and 98% respectively[9].

Material and method: - This study was conducted in S.M.H.S Hospital and Govt. Dental College Hospital Srinagar. The persons for the study were chosen among doctors from Surgery Department, persons working in Operation Theatre, Endoscopy Staff, Dental Surgeons, Nurses, Sweepers and Medical Students. Study enrolled 150 professional workers and 50 non-professional persons of same age and sex. A detailed clinical history regarding smoking, alcohol, dietary habits, source of drinking water, present and past medical history with particular reference to indigestion, heart burn, acid erucation or epigastric pain, family history and previous investigations like barium studies stomach, upper GI endoscopy, ultra sonography, and previous use of antiulcer drugs and anti H.pylori treatment was taken. A detailed general physical and systemic examination was done with particular reference epigastric tenderness, mass, ascites, gastric splash, hepatosplenomegaly. Investigations like blood sugar random and E.C.G was done in all cases. The venous sample of blood was taken from median cubital vein. The serum was assayed for anti H.pylori antibodies.

The results were calculated as:

Results: - The age cases (professional workers) ranged from 20 – 56 years with (mean ISD = 35.96 ± 8.66). The age range among controls was 20 – 65 years with (mean ISD = 39.04 ± 12.54). Among cases 64% were males and 36% were females.

Among controls 62% were males and 38% were females. 40% cases were smokers and 60% were non-smokers. 64% cases were positive for Ig G anti H.pylori antibody among professional workers and 48% among control group (P<0.05). H.pylori seropositivity had a positive corelation with age, being highest in the age group of 36 – 65 years (72% – 78%) and lowest in the age group of 20 – 35 years (57.44%). In cases higher value of H.pylori seropositivity was found in each group in males as compared with females seropositivity differed significantly between two sexes except in age group 20 – 35 years were seropositivity was more for females (P>0.60). Out of 150 cases the history of gastrointestinal symptoms were present in 86, among whom 62 (72.10%) were H.pylori seropositive. Out of 64 asymptomatic cases 31 (47.82%) were seropositive for H.pylori (P<0.01). The seropositivity in different professional workers showed a stastically significant difference in endoscopy staff and dental surgeons (P<0.051). The results showed an increasing positivity of H.pylori with increasing duration of work, but the difference was stastically non-significant (P>0.20). Among professional workers seropositivity was found in 75% of cases belonging to poor families while as it was 54% in cases belonging to good socioeconomic status (P<0.05). Our study also showed H.pylori positivity 50% and 70% in 3rd year and final year MBBS students respectively.

Discussion: - This study was carried to find out the prevalence of H.pylori seropositivity among professional workers in main teaching hospitals of Kashmir Valley. All the cases were randomly selected from different departments all the cases and controls were subjected to H.pylori Ig G ELISA test detection of Ig G antibody in the serum is a sensitive and specific method for studying the epidemology of H.pylori infection in healthy population in whom endoscopy is not indicated. Our study which used ELISA method to detect the prevalence of H.pylori infection found a significantly higher positivity rate in professional workers (64%) as compared to control group 48% (P<0.05).

The prevalence of H.pylori infection increased after the age of 35 years in our study having a positivity of 75%. Those observations are in accordance with that made by Presecki (1977)[10], Graham DY etal[11]. The difference in prevalence between two age groups may be caused by two different mechanisms, an age effect or a cohort effect. The older subjects in the study could have a higher prevalence of infection either because they have lived longer and hence have had more opportunity for infection or because they were born at a time when the risk of infection in childhood was higher than those born later. Higher prevalence of H.pylori seropositivity was found in each age group in males as compared to females. In case group, seropositivity differed significantly between two sexes except in age group 20 – 35 years. In whom it was more for females (P>0.60). This does not confirm with what has been reported by Rudial etal in 1997[12] who in his study showed that anti H.pylori antibodies were present more frequently in women than in men. The factors for the difference in prevalence in different socioeconomic groups include hygiene environmental contamination, standards of living and sanitation practices. Recently published epidemiological data showed that the prevalence of infection in children was associated with the source of their drinking water. This association between consumption of water and H.pylori infection suggests that under appropriate circumstances H.pylori may be transmitted by a water born route[9]. The H.pylori positivity in endoscopy workers as compared to controls was 80% Vs 48% (P<0.051) similar observations have been made by Abbas etal[9], KL Goh (1996)[13]. These findings of an increased prevalence of H.pylori infection in endoscop staff performing endoscopy support human to human transmission, possibly from patient to medical staff. The likely reason could be the lack of use of gloves or self contamination as a result of close proximity of the biopsy port to the mouth, or due to handling of improperly disinfected endoscopes. The 60% positivity of H.pylori in nurses working in both medical and surgical wards of S.M.H.S Hospital was identical to that of Presecki etal 1993[15]. The increased risk of infection is an increased exposure to faeces and exposure to nasogastric tubes. The H.pylori seropositivity was 60% and 68% in persons working in different operation theatres and general surgeons respectively. This observation goes in favour of the earlier reported observation by Mones etal (1999)[14]. The high prevalence of H.pylori positivity is due to easy access to the stomach during abdominal operations. Our study showed stastically significant difference in H.pylori positivity rate in dental surgeons as compared to controls 76% Vs 48% (P<0.05). Majmudar P etal (1990)[9] looked presence of H.pylori by CLO test, culture and warthin starry stain in all 40 healthy volunteers entitled in study 100%. Our observation is supported by this study human and animal stomachs were considered the only reserviors of H.pylori until it was identified in human dental plague. H.pylori is infrequent in populations from developed countries, but is wide spread in those from developing countries. The failure of treatment therapy to eradicated H.pylori from dental plague, despite its clearance from gastric mucous raised the possibility of dental plague as a permanent reservoir of H.pylori and is potential source of reinfection of gastric mucosa[16,17]. High prevalence in final year medical students is possible because they are more exposed to nasogastric secretions, patient exposure as compared to third

year medical students. We tried to find out a correlation between H.pylori positivity and the duration of work in profession, although the positivity rate showed an upward trend with increasing duration of work, the differences were not stastically significant (P>0.20). Similar observations were found by Lin SK etal (1994)[18], who stated that prevalence of H.pylori infection in gastroenterology nurses increases with years of practice.

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Autosomal Dominant Polycystic Kidney Disease and Nephrolithiasis in a Horseshoe Kidney A Case Report

Bakshi Jehangir, Omar Kirmani, Sajjad Dar

Abstract

The authors present a rare case of Autosomal Dominant Polycystic Kidney Disease and nephrolithiasis in a horseshoe kidney.

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Horseshoe Kidney is a renal fusion anomaly in which both kidneys are fused together in early embryonic life. In more than 90% of cases, fusion occurs along the lower poles with the region of fusion, called the isthmus, being composed of renal parenchymal tissue. The reported incidence of horseshoe kidney varies from 1 in 400 to 1 in 1,800 live births.[1,2]

Autosomal Dominant Polycystic Kidney Disease (ADPKD) also known as **Adult Polycystic Kidney Disease** is a hereditary disorder with autosomal-dominant transmission. Cysts arise from the nephrons and the collecting tubules with islands of normal parenchymal renal tissue interspaced between the cysts. About 85% are designated as PKD1 with an abnormality on chromosome 16 and 15% are PKD2 with an abnormality on chromosome 4. Its incidence is approximately one in every 1,000-5,000 cases[3].

Polycystic Horseshoe Kidney is a very rare entity with an incidence ranging from 1 in 134,000 to 1 in 8,000,000 cases.[1,4]

Diagnostic criteria for ADPKD1 were established by Ravine et al[5] in 1994 and are as follows:

- At least 2 cysts in 1 kidney or 1 cyst in each kidney in an at-risk patient younger than 30 years
- At least 2 cysts in each kidney in an at-risk patient aged 30-59 years
- At least 4 cysts in each kidney for an at-risk patient aged 60 years or older

Ultrasound is the modality of choice for imaging the urinary tract. It can detect cysts as small as 1 to 1.5cm in diameter. Sensitivity for PKD1 is 100% over the age of 20 but false negatives can occur below this age. It is also possible to scan other organs like the liver or pancreas for cysts. CT is more sensitive for smaller cysts but the diagnostic value has to be balanced against the high radiation dose.

We present a case of ADPKD and nephrolithiasis in a horseshoe kidney in a 22 year-old female with family history of ADPKD, who was investigated by **Ultrasound [USG]** and contrast-enhanced **Computerised Tomography [CECT]**.

The **Ultrasound** scan revealed multiple cysts in both kidneys and a calculus with acoustic shadowing in the right kidney. Contrast-enhanced Computerised Tomography images showed horseshoe kidney fused at the lower pole with multiple cysts seen in both moieties. The isthmus spanning both moieties was clearly demonstrated by CECT. There was no evidence of Hepatic cysts, or any cerebral or cardiac abnormalities.

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Key words: Polycystic Horseshoe Kidney, Authosomal Dominanant Polycystic Kidney Disease (ADPKD), Nephrolithiasis

Fig. 1. — USG image showing hyperechoic calculus with acoustic shadowing.

Fig. 2. — CECT image showing isthmus (arrow) spanning both lower poles of kidneys and multiple cysts in right moiety.

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Fig. 3. — CECT image reveals bilateral multiple cysts and calculus (arrow) in right moiety.

Fig. 4. — CECT image demonstrating bilateral multiple cysts of Autosomal Dominant Polycystic Kidney Disease.

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Necrotizing enterocolitis in a very low birth weight (VLBW) neonate.

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Abstract

A case of necrotizin enterocolitis in a pretem body of 26 weeks gestationalage, weighine 800 grams in presented here. Neonatal Necrotizing Enterocolitis (NEC) is the most common life threatening emergency of the gastrointestinal tract in the newborn period.This disease is of unknown cause that predominantly affects premature infants.

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Although the initiating events in the pathogenesis of NEC have not been established, there are various epidemiological observations that emphasize the potential role of infection, enteric feeding and local gastrointestinal vascular compromise in the causation of the disease.In the past quarter century, NEC has become the most common neonatal abdominal condition requiring emergency surgery and has also emerged as the leading cause of mortality in surgical neonates. Improvement in the outcome of infants with NEC most of whom are very low birth weight (VLBW) babies require close cooperation between Paediatric Surgeons and Neonatologist to ensure early detection, timely intervention and appropriate after care of the condition.

Preterm, female baby born to 30 years old multigravida mother (Gravida six, para zero – all the five were abortions). This 30 years old mother was investigated for bad obstetric history in higher medical centers both inside and outside the country, and was diagnosed as a case of bicornate uterus and antiphospholipid syndrome. Taking small dose of aspirin, she did not remember her last menstrual period. She was admitted for premature rupture of membranes with water discharge for two days and received antibiotics and two doses of Dexamethasone.

On examination gross preterm baby with a gestational age of 26 weeks, weight 800 grams, length 32 cm. and head circumference 26 cm. Apgar score of 5&6 at 1&5 min. developed respiratory distress and needed assisted ventilation. Both umbilical central lines were inserted, septic screening done and antibiotics (Ampicilin & Gentamycin) started. Blood gases were normal on low ventillatory settings. Chest x-ray showed mild hyaline membrane disease. Total parenteral nutrition was started on day two and was continued for 2 weeks. Nasogastric tube feeding (NGT) was started on day five after removing arterial catheter with expressed breast milk and formula feed. In view of clinical picture (lethargic with skin mottling), sepsis was suspected, septic screening done. Antibiotics were changed to Amikacin and Ceftazidine. Blood culture revealed streptococcus epidermis and responded to the treatment. Antibiotics were stopped after one week, and repeat blood culture yielded no growth. On day ten, patent ductus arteriosus was suspected in view of bounding pulses and systodiastolic murmur and confirmed by the Paediatric Cardiologist. The ductus closed by conservative management (fluid restriction and diuretic) and confirmed by echocardiogram. At the age of 3 weeks, patient needed high ventillatory settings. Chest x-ray revealed pneumonic consolidation. Tracheal aspirate revealed Methecillin resistant staphylococcus aureus (MRSA). After the treatment the patient improved. She developed seizure and was controlled with inj. Luminal. No cause for seizure could be detected. Ultrasonography of the brain was normal.

The baby was extubated at the age of one month, by this time she was on full NGT feeding. At five weeks of age, she developed abdominal distension and passed blood with stool, and started to become lethargic. There were also palpable loops of bowel in the abdomen,(figure 1.) The abdominal x-ray revealed intramural gases in the intestine .Based on these findings she was operated where grossly dilated small and large bowel loops were found, with edema and hemorrhagic patches in the small intestine and peritoneum,(figure 2) Loop ileostomy was done. After improvement feeding was resumed and the patient

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Key words: *neonate, necrotizing enterocolitis , preterm*

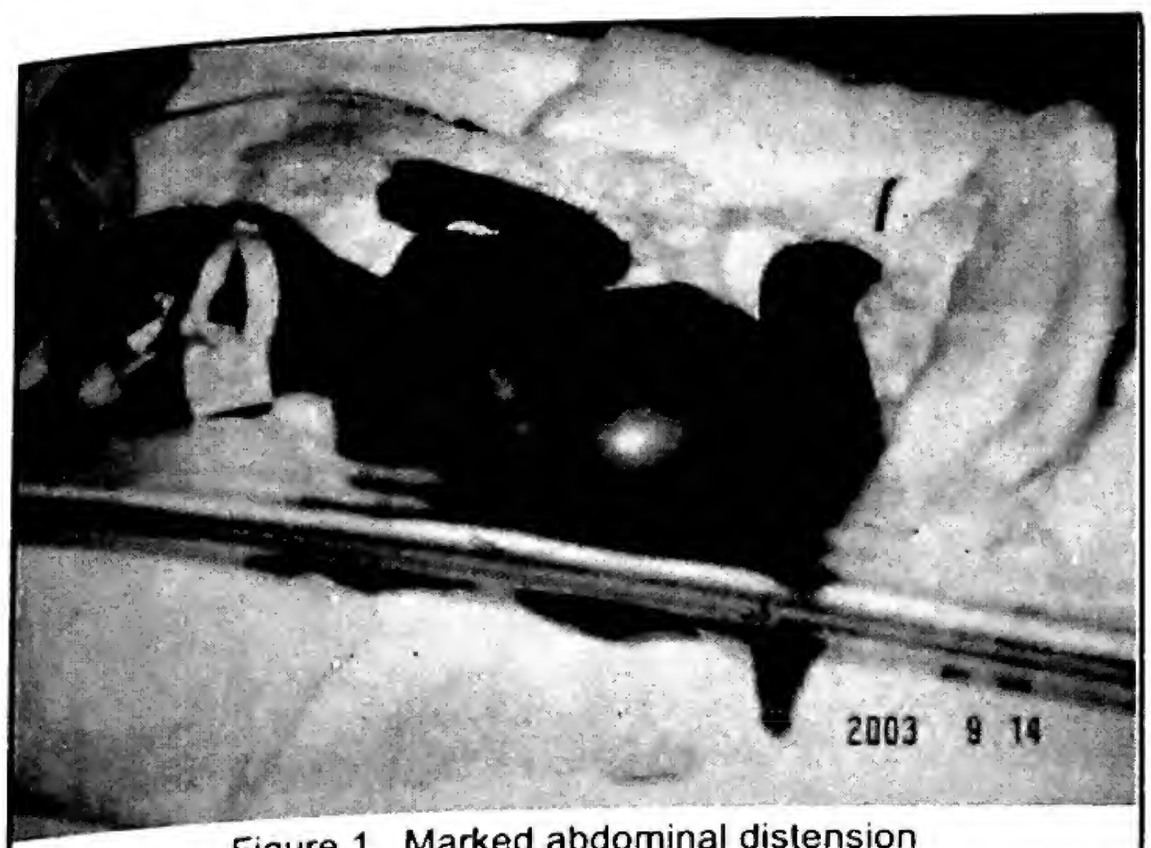

Figure 1. Marked abdominal distension

Page 101

Fig. 2. Distended and inflammatory bowel.

Page 101

Fig 3.Same child at the age of two years.

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started gaining weight.

At the age of 9 weeks, the clinical picture was suggestive of sepsis, and blood culture yielded enterobacilli, treated with appropriate antibiotics. In view of hyponatremia, weight gain was slow and after correction the patient started gaining weight. Mother was kept in rooming in for the care of the baby and was eventually discharged in a good condition. The parents were explained the nature of the disease and possible late complications. At the age of three months, weight was 1.8 kg. Second stage surgical intervention was done at the age of eight months, where the ileostomy was closed. A preoperative contrast study of the distal bowel was done which excluded presence of strictures. She regularly attends follow-up clinic and her developmental assessment revealed normal vision and hearing although her motor functions and language is delayed. (Fig. 3).

Discussion

The clinical and pathological features of NEC in the newborn were described in 1891 but for 60 years or more, the diffuse picture of the disease was interpreted as multiple conditions. The term NEC was used by Cruze & Synder in 1961, but it was Waldhausen, Herenoun and King who first clearly described the disease in 1963.

Increased incidence of Necrotizing Enterocolitis (NEC) in recent years is believed to be due to better neonatal care and survival of premature and very low birth weight babies. Among preterm babies the incidence of NEC is inversely proportional to the gestational age. Preterm neonates are known to have decreased gastric acid secretion, decreased proteolytic enzyme activity, poor intestinal motility, reduced secretary IGA, and reduced T cell numbers and increased mucosal permeability. All these operate in to create intestinal host defense deficiencies, thus facilitating bacterial overgrowth and obstruction of the infected intestinal epithelial cells.A high index of suspicion in recognizing infants at risk is essential. Intensive therapy is advised for suspected as well as diagnosed cases. The Paediatric Surgeon should be involved early in the course of management. Indications for earlier surgery for NEC with a good outcome includes the combination of deterioration in the clinical condition of the patient with a palpable mass of loops of bowel which are seen as a persistently dilated loops on sequential X-rays . Each of these factors specially when associated with persistent metabolic acidosis and thrombocytopenia, suggest the existence of a necrotic loop of bowel and impending perforation. Still some neonatal units worldwide consider perforation and pneumoperitoneum as the only indication for surgical intervention in NEC patients. Mortality rates vary across centers and range from 10-14% depending on gestational age of the baby. Those who survive may have significant complications both in short and long term including neurodevelopment. Attempts to prevent NEC focus on minimizing the multiple contributing factors in a susceptible host including correction of hypovolemia and hyperviscosity. Signs of feeding intolerance increase in gastric aspirates, abdominal distension and haem positive stools. Evidence of feeding dysfunction mandates close observation and may require reinstitution of intravenous support and intestinal decompression. Total parenteral nutrition has dramatically improved the management of gross preterm babies and NEC.

Evidence shows that TPN facilitates intestinal adaptation by promoting hypertrophy and dilatation. Before an infant who survived NEC is discharged home, all current and anticipated medical and developmental concerns must be identified and communicated to the infant's parents. There is additional risk for developing bowel obstruction secondary to adhesions. Bowel obstruction develops in at least 5% of patients who have had abdominal surgery for NEC. Till date none of these

complications were observed except language and motor mile stones in our case.As the disease is more common in preterm and formula fed neonates,efforts should me made to prevent the premature deliveries.More stress should be laid on the use of breast feeding .

We are thankful to the staff of the Department of neonatology for their cooperation. Thanks are also due to DR. Zakaria Hawasawi consultant Pediatrician Department of Pediatrics Madina Maternity & Children Hospital for the clinical assistance.

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Unusual Complication of feeding jejunostomy, Feeding catheter induced jejuno-jejunal Intussusception.

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A 50 years old male underwent transhiatal oesophagogastrectomy for carcinoma Gastro-esophageal junction. Feeding Jejunostomy was performed as part of the procedure. On 7th post operative day patient developed upper abdominal pain and anastomotic leak. Patient was re-operated, jejuno-Jejunal Intussusception causing Intestinal Obstruction and anastomotic leak from Oesophagogastostomy site was found. Placement of feeding jejunostomy a an adjunct to upper gastrointestinal surgery is a widely accepted phenomenon because of the established advantages of early entral feeding. However, feeding Jejunostomy may lead to serious complications with lot of morbidity and mortality [1]. We present this case of ca. esophagus who was to be re-operated because of feeding jejunostomy catheter balloon induced small bowel intussusception and intestinal obstruction.

The concept of feeding Jejunostomy was Ist given by Delany at all in 1973[2] and it is routinely performed in our department following Oesophasgogastrectomy .Use of feeding Jejunostomy is now widely accepted.

However complications of feeding jejunostomy are seldom reported. To develop a reasonable policy regarding this specific feeding access it is important to specify the technical complications. The various complications reported due to feeding jejunostomy are pain, intraperitoneal leakage, tortion, herniation, dislodgement strangulation and small bowel necrosis. Mortality of 0-1.4% has been reported in different studies[3-6] However, feeding jejunostomy is of tremendous importance especially in our set up of low socio economic status where patient present with significant weight loss. It is cheap, easy to manage postoperatively and is a "safety net" for those patients who are at the risk of developing complications postoperatively.

JK-Practitioner 2006;13(2):103

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Eclipse Retinopathy

Afroz A. Khan MS; Manzoor Qadir Keng MS; Sabiya Rashid MS

A 15 years old boy reported to the Out patient clinic of Ophthalmology department with complaints of blurring of vision and metamorphopsia in both eyes immediately after viewing the solar eclipse for a brief period through a mirror.

On examination the visual acuity recorded in both eyes was 6/18. slit lamp examination was normal. Funds examination of both the eyes showed a small yellow spot with a surrounding grey zone (Fig. 1 and Fig. 2). Fundus fluorescein angiography was normal in both eyes. The patient was put on topical ketorolac (0.5%).

At three months follow up the patient was asymptomatic. His visual acuity in both eyes was normal (6/6) and so was the foveal appearance.

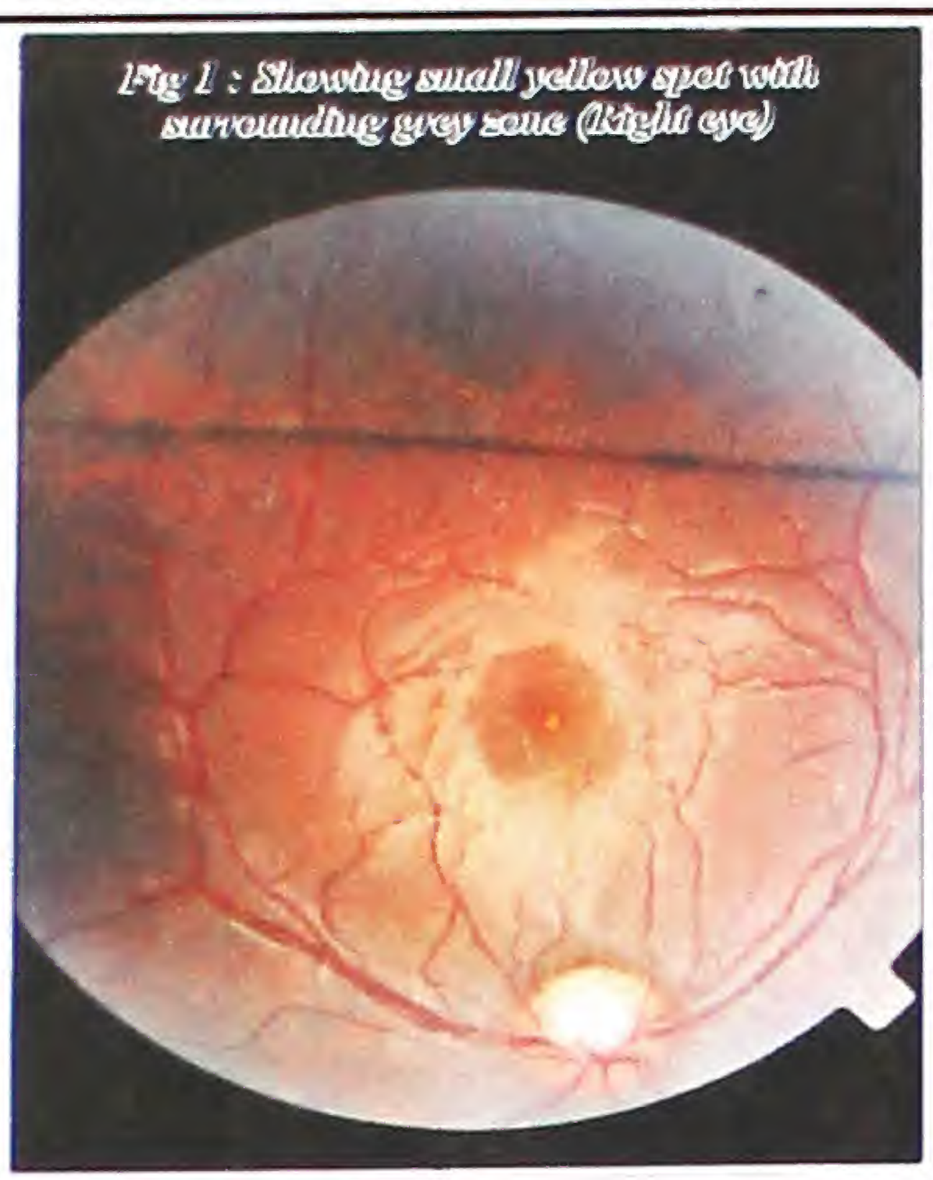

Fig 1 : Showing small yellow spot with surrounding grey zone (Right eye)

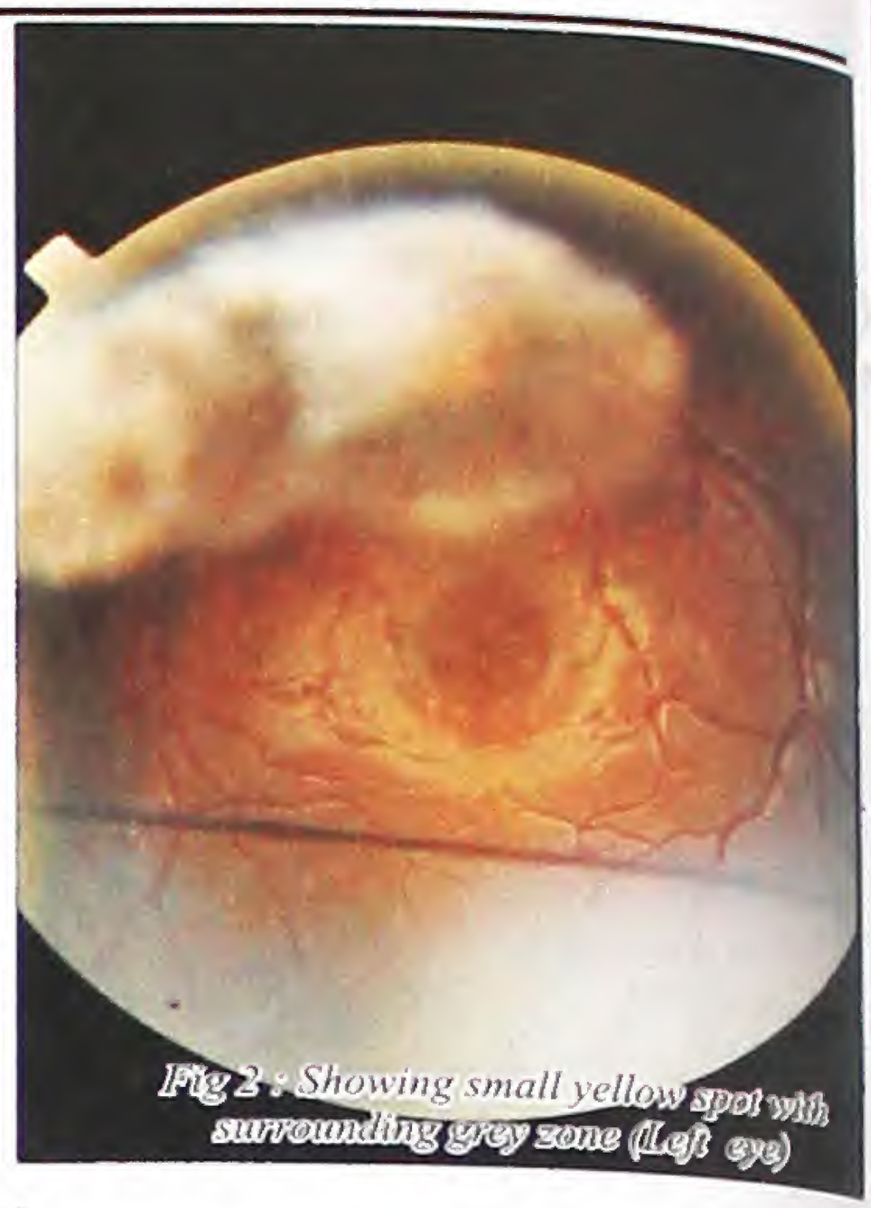

Fig 2 : Showing small yellow spot with surrounding grey zone (Left eye)

A causal relationship between solar observation and eye damage dates back to many centuries. Galelio reportedly sustained retinal injury by viewing the sun through telescope[1]. The clinical presentation of eclipse retinopathy is well described[2]. Ocular involvement is usually bilateral as in our patient. Like in our patient, young people because of their adventurous nature and transparent crystalline lens are at increased risk of developing solar retionopathy[3]. It has been reported that severity of retinal lesions is related to the duration of exposure[4]. However the exposure to solar eclipse in our patient was brief and through a mirror, producing equally significant lesions. This could be explained by variability in the degree of susceptibility to photic damage which has been already established[5]. The typical fundus lesion described in eclipse retinopathy is a small yellow spot with surrounding grey zone in the fovea within first few days of exposure followed by recovery[6]. Our patient also exhibited the typical fundus lesion followed by complete recovery.

CONCLUSION

Solar eclipse retinopathy is a self limiting disease, which effects both eyes followed by complete recovery. Viewing an eclipse through binoculars, sunglasses and photographic or radiographic films is not safe. Use of solar filters and public awareness can be helpful in preventing retinal injury.

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Accidental Bilateral Ureteric Ligation during Abdominal Hysterectomy and excision of a pelvic mass

Basher Ahmed Lone

A 45-year-old female was reffered to Sher-i-Kashmir institute of medical sciences, Srinagar from L.D hospital for the treatment of anuria following total abdominal hysterectomy and excision of a pelvic mass. Anuria persisted despite fluid challenge. Her blood urea nitrogen and serum creatinine was raised. Further evaluation with ultrasonography and CT showed swollen kidneys, dilated ureters and empty bladder. There was haemorrhagic fluid in the abdomen.

On exploration there was about one liter of blood in her peritoneal cavity. Both the ureters were grossly dilated and kidneys were enlarged. Both the ureters were found ligated and engulfed in the uterine pedicle near vesicoureteric junction. Right uterine pedicle was bleeding.

Blood was evacuated from abdominal cavity and right uterine pedicle was suture ligated. Both the ureters were transected near vesicoureteric junction and reimplanted into the bladder.

She had normal postoperative period and was discharged on 8th day of surgery She got wound disruption at home on 12th post operative day and was resutured. She is under regular urological follow up and is doing fine.

Ligation of a ureter is a form of iatrogenic extrinsic obstruction of ureter. Majority of such injuries occurs during various gynecological procedures.

During routine hysterectomy its incidence varies from 0.5 to 3% but is bilateral in 1 out of every 6 such cases Its incidence is 10 to 15% following radical hysterectomy.

Ureter is damaged commonly in (1) ovarian fossa (2) infundibulo pelvic ligament (3.) where ureter and uterine artery cross and (4.) vagino-vaginal canal. Bilateral Ureteric obstruction also occurs in retroperitoneal fibrosis, pregnancy,Pelvic lipomatosis, ca cervix and aortic aneurysm etc. Diagnosis is made by careful history, general physical examination and careful evaluation of genitourinary system, vascular system and gastrointestinal system.

Bilateral Ureteric obstruction is a surgical emergency and needs immediate Surgical intervention. [1-4]

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Dialysis and the Kashmir Scenario

M. Saleem Najar, M. Ashraf Bhat

Dialysis took off in the state of Jammu & Kashmir in late 1982 with the installation 4 hemodialysis machines and start of Acute Peritoneal Dialysis. The next centre came up years later at Government Medical College, Jammu and a small facility in private sector in the city of Srinagar. Except for introduction of Continuous Ambulatory Peritoneal Dialysis at Sher-i-Kashmir Institute of Medical Sciences, Srinagar in the year 2000, not much progress could be made as far as the state is concerned. At present all the forms of dialysis are well established at Sher-i-Kashmir Institute of Medical Sciences, Srinagar and a vast expansion is very eminent there. Still the question is whether we are anywhere near the actual target?

Incidence of end-stage renal disease (ESRD) in the United Kingdom varies between 80 and 110 new patients per million of population and 315 in the United States of America.[1] Incidence of ESRD at Sher-i-Kashmir Institute of Medical Sciences, Srinagar is 60, (Unpublished data). It is clear that the prevalence of ESRD is much higher in the state of Jammu & Kashmir. The available renal replacement therapy in the form of kidney transplantation, hemodialysis and continuous ambulatory peritoneal dialysis in the state at the moment can at most cater to only a small number of these patients. While in kidney transplantation and continuous peritoneal dialysis organ shortage and cost factor respectively are proving big hurdles, a quick and vast expansion of hemodialysis facilities is the need of the hour.

Dialysis involves movement of molecules across a semi permeable membrane. Clinically, this movement takes place in an out of blood. If the blood is exposed to an artificial membrane outside the body , the process is called hemodialysis (HD) or hemofiltration. If the exchange of molecules occurs across the peritoneal membrane, the process is called Peritoneal Dialysis (PD).[1]

Before 1970, patients with end-stage renal disease (ESRD) had only one prognosis-death as only a very small number of patients were receiving regular dialysis because few dialysis centers had been established. Despite advances in knowledge and skill in treating chronic kidney disease (CKD), patients with end-stage renal disease remain unwell even when maintained by regular dialysis. Constitutional symptoms of fatigue and malaise persist despite the dramatic improvement that followed the introduction of erythropoietin for the management of anemia of CKD. Progressive cardiovascular disease, peripheral and autonomic neuropathy, bone disease and sexual dysfunction are common even in patients who receive adequate amounts of dialysis as judged by established objective criteria (Urea Reduction Ratio and Kt/V from Urea Reduction for HD and Weekly Createnine Clearance and Residual Glomerular Filtration Rate for PD).[2] However, such findings are not unexpected, because the most efficient hemodialysis regimens currently provide only 10% to 20% of the small-solute (i.e. urea and creatinine) removal achieved by two normally functioning kidneys. Removal of higher molecular-weight solutes (i.e. middle molecules) is even less efficient. It is pertinent to mention here that peritoneal dialysis is less effective than hemodialysis. For more patients with ESRD, kidney transplantation offers the greatest potential for restoring a healthy, productive life. However, clinical effects of ESRD on the overall health of renal transplantation patients throughout what may be decades of successful post-transplant clinical follow-up, must be kept in mind.

In ESRD population men slightly out-number women. Despite improvements in clinical management of both diabetes mellitus and hypertension, these two diagnostic categories remain the most common cause of ESRD. In contrast to the steady rise in the number of patients receiving regular dialysis, the number of patients receiving kidney transplantation in the United States of America has only marginally increased and against about 15000 transplantations (both cadaver and live) in USA only about 2500 kidney transplants are performed per year in India. The main reason for this situation is the supply and the demand for kidneys.[3]

Hemodialysis is the predominant method for treating ESRD throughout the world. It can be done in a hospital setting or at home and always needs a trained attendant. Usually four hours per session dialysis is given thrice a week. During dialysis solutes are removed by diffusion across a semi permeable membrane within a dialyzer (artificial kidney) from blood circulated through an extra corporeal circuit. Extra fluid can be removed by ultra filtration. The intermittent nature of HD, which results in rapid changes in extra cellular fluid volume, blood solute concentration and plasma osmolality, may contribute to post dialysis fatigue and malaise.

HD is generally well tolerated, although ultra filtration can cause hypotension, nausea and muscle cramps. Older patients and those with established cardiovascular disease may tolerate the procedure less well. Vascular access failure from the repeated cannulations and the need for intermittent heparinization to prevent clotting in the extra corporeal blood circuit are additional concerns, particularly in diabetic patients. With respect to their effects on patient morbidity and mortality, concerns regarding dialysis efficiency and adequacy have received lot of attention.

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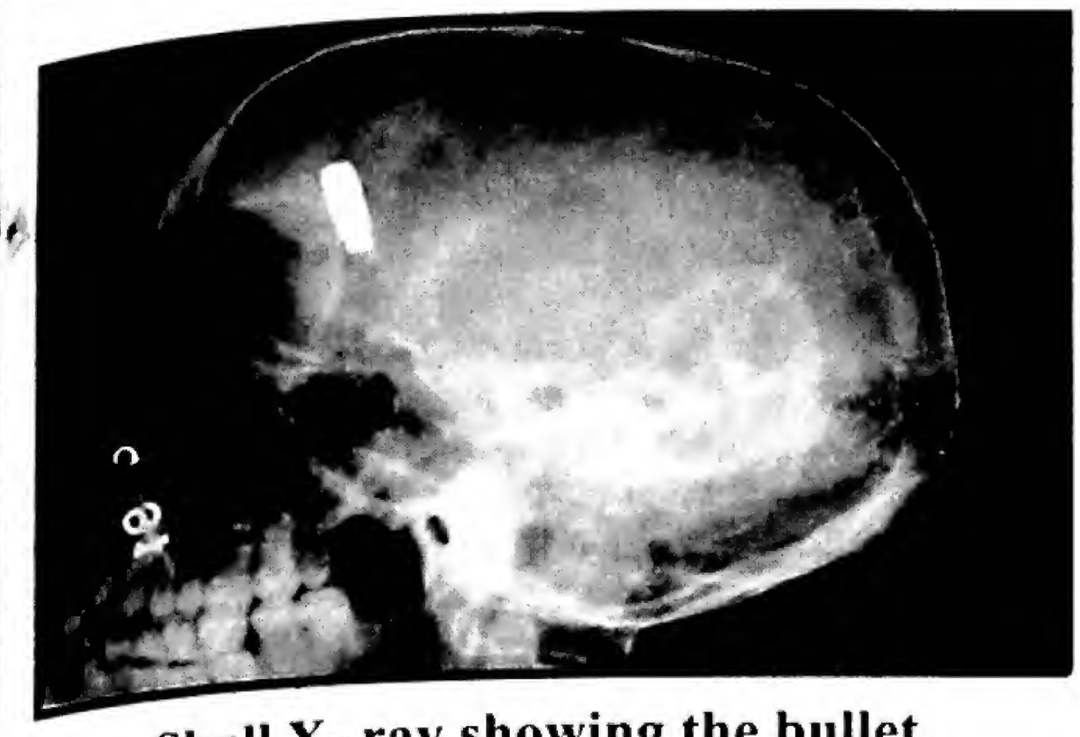
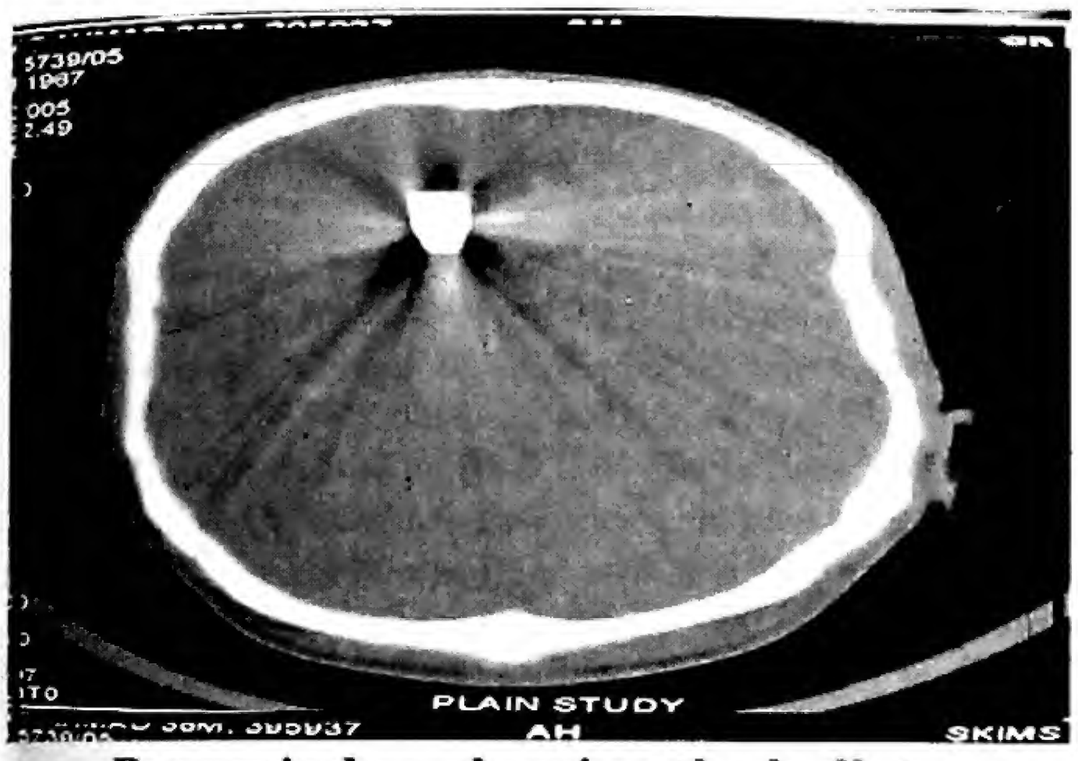
Neuroimage

Khursheed N M Ch, Shafiq A MS; Rumana M MD; Ramzan A M Ch;



Skull X- ray showing the bullet

CT scan head showing bullet in the left frontal area with streak artefacts.



Bone window showing the bullet.

And Adult male was hit by a stray bullet in his frontal area. On reception in AE he was consciuos, alert, had no neurodeficits. He had an entry wound in left frontal area. There was no active bleed from the wound. He underwent emergency wound debridement and duraplasty after skull X-ray and CT scan. Further management for removal of the bullet is to be planned.

Gunshot wounds of head account for majority of penetrating brain injuries and comprise about 35% of deaths from brain injuries in person < 45 Years[1]. In penetrating head injuries fracture lines pass from the entry wound to the exit wound[2]. The importance of wound debridement, dural repair, removal of accessible missiles, antibiotic therapy has been accepted since world war II [3,4,5].

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Dialysis: Design and Construction of Dialysis Units.

Ghulam Jeelani Qadri, M. Saleem Najar, M. Ashraf Bhat

Dialysis: The earliest known theories and attempts to create an artificial kidney machine came about in the late 1800's. In 1861 Thomas Graham coined the word Dialysis (from Greek "dia" meaning through and "lysis" to loosen), a term which stood the test of time. He tied parchment around a hoop floating in water. Into this hoop-dialyzer he placed solutions of colloids and crystalloids and demonstrated that only crystalloids passed through the membrane.

In 1913 Abel, Rowntree and Turner · devised an apparatus for hemodialysis and performed it on experimental animals.

In 1925 Dr. Hass · in Germany performed first recorded hemodialysis on patients with renal failure using hirudin as an anti-coagulant. Hirudin was found to be unsafe and heparin, another anti-coagulant, was discovered in 1922.

In 1937 Thalhermer attempted to use heparin and cellulose acetate, a membrane used in sausage industry, in the procedure and in 1938 intermittent peritoneal dialysis was first used to treat patients with chronic renal failure.

In 1943, Wellen Kolff made a major breakthrough by developing an artificial kidney machine in Holland. He used a rotating drum around which a membrane of cellulose acetate sausage skin was wound. Year 1945 saw, for the first time, a patient treated with the artificial kidney, recovering from a temporary shut down of kidney function due to illness. · And in 1947 Kolff brought the artificial kidney to United States. In 1948 first dialysis procedure was performed on a patient in the United States at Mount Sinae Hospital in New York City. Dr. John Merrill at Peter Bent Brigham Hospital led a study team that improved the rotating artificial drum. Further development took place and first dialysis unit for chronic renal failure patients, the first large scale Hemodialysis Programme, was initiated at Long Island College Hospital in Brooklyn.

However, problems of vascular access limited the use of dialysis to patients with acute renal failure who only needed renal replacement therapy for a short time. In 1960, arterio-venous cannula system was introduced as vascular access for hemodialysis by Belding H. Scrcbner in Seatle in United States. ·

In 1965 Brescia and Cimino · developed a sub-cutaneous arterio-venous fistula (A-V fistula). The fistula (internal) eliminated the problems of infection, clotting and erosion of overlying skin inherent in the external arterio-venous shunts.

In 1966, the hollow fiber dialyzer was developed and represented a great improvement over pervious versions.

Ganter (1923) · initiated several animal and human studies on peritoneal dialysis and enunciated many of the principles that are still true today. The modern era of clinical peritoneal dialysis started in 1959 with the introduction of simplified method based on intermittent irrigation of the peritoneal cavity using a single, disposable catheter and commercially prepared dialysis solution (Maxwell et al 1959). · However, repeated puncture, peritonitis and lower efficacy in comparison to hemodialysis limited its use in patients with terminal renal failure.

A major advance came in late 1960s when Teuckhoff and Schechter (1968) · reported on the use of a permanent, indwelling, silicon-rubber catheter with two decron cuffs. But this 'periodic' intermittent peritoneal dialysis was regarded as having little place in the treatment of the patients in end-stage renal failure despite its efficacy. The situation changed dramatically after 1976 when Popovich et al (1976) · introduced the concept of a portable/wearable
equilibration peritoneal dialysis technique. This new approach, resulting in steady-state, low blood concentrates of uraemic metabolites, was later developed into the currently accepted continuous ambulatory peritoneal dialysis (CAPD).

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Advancement in peritoneal catheters, devices to decrease contamination during exchanges and development of automated equipment continued into the 1990s to make peritoneal dialysis more efficient.

In the 1980s-1990s, computerized hemodialysis machines, better dialyzers and improved monitoring and safety devices reduced treatment times, gave doctors better ways to moniter treatment and made possible a more normal life for patients. In 1989 a major break through was the introduction of erythropoietin to combat anaemia in dialysis patients and give new energy and stamina to these patients. Due to the many advancements made in dialysis therapy, patients can now lead healthier, more normal lives.

Today more than 1.3 million people around the world are being kept alive by hemodialysis and about 0.15 million by peritoneal dialysis.

Dialysis techniques

1. Peritoneal Dialysis
2. Hemodialysis

Peritoneal Dialysis:

a. Intermittent Peritoneal Dialysis: This has a major use in acute renal failure, hyperkalemia and volume over-load states. It is simple and can be performed even at remote places, can be done manually or by a machine. In manual method 20-30 ml dialysis fluid per Kg body weight is used per exchange. This fluid dwells in the peritoneal cavity for about 20 to 30 minutes and 20 to 30 exchanges are carried out. A hard catheter is placed through a small nick in the skin in the peritoneal cavity for the period of dialysis only. Exchanges can be performed by a dialysis machine (cycler) automatically also.

b. Continuous Ambulatory Peritoneal Dialysis (CAPD): It is done as renal replacement therapy for end-stage kidney failure. It is continuous; machine free and done while one goes about his normal activities. Here the dwell time is long and 3 to 5 exchanges are done per 24 hours every day.

c. Continuous Cycling Peritoneal Dialysis (CCPD): It is done as renal replacement therapy in end-stage renal failure. CCPD differs from
CAPD in that a machine (cycler) delivers and then drains the cleansing fluid for the patient. The treatment is usually done at night while the patient is asleep.

Hemodialysis

Components:

1. Circulatory access,
2. Dialyzer,
3. Method for Anticoagulation,
4. Dialysate delivering equipment,
5. Monitoring equipment,
6. Water Treatment, and
7. Blood pump.

It is done usually thrice a week for four hours in one session. It is common mode of maintenance dialysis and is usually performed in a hospital setting but home dialysis is also possible. It needs an attendant always.

Different Hemodialysis Techniques are:

1. Traditional Hemodialysis,
2. Hemofilteration,
3. Hemodiafilteration, and
4. Ultra-filteration.

1. Traditional hemodialysis: Here blood flows on one side and the dialysate on the other side of a dialyzer membrane. To maximize solute movement, the blood and dialysate flow in opposite directions (counter current flow). In this technique, diffusion is a predominant method of solute clearance.

2. Hemofiltration: This technique employs a large quantity of hydrostatic ultra-filtration. Plasma ultrafiltrate is replaced with plasma-like electrolyte solution. Solute removal is achieved by convection (solvent drag) and volume control by the difference between the volume removed and the volume replaced.

3. Hemodiafiltration: In order to improve solute clearance, hemofiltration (convective transport) may be combined with diffusive transport by allowing dialysate to flow on the ultrafiltrate side.

4. Ultra-filtration: If the volume removal only is needed, it can be achieved by intermittent ultrafiltration or slow and continuous ultrafiltration, without replacement of ultrafiltrate.

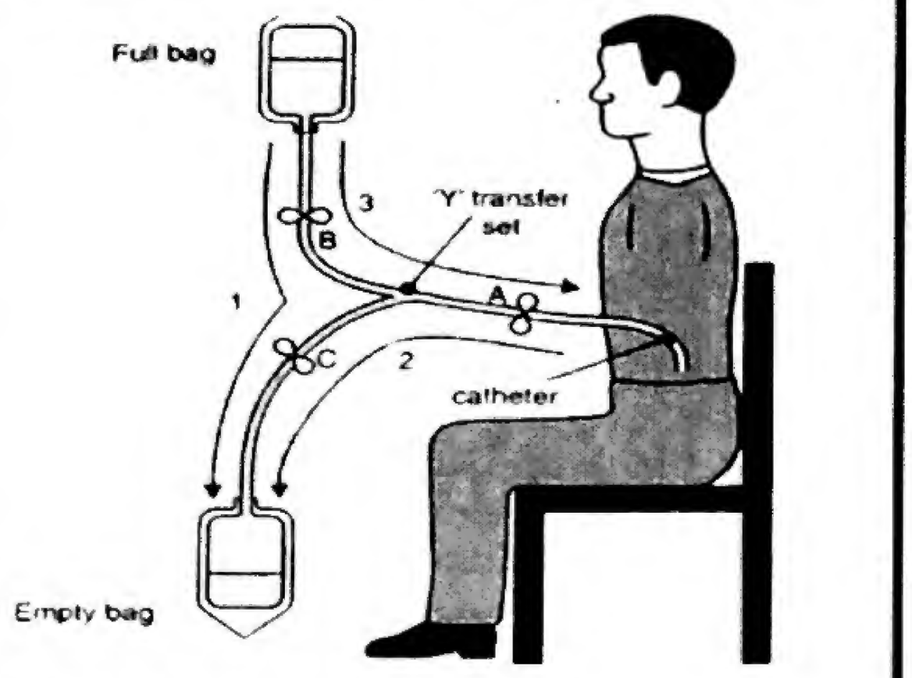
DESIGN AND CONSTRUCTION OF A DIALYSIS FACILITY.

The steps are:

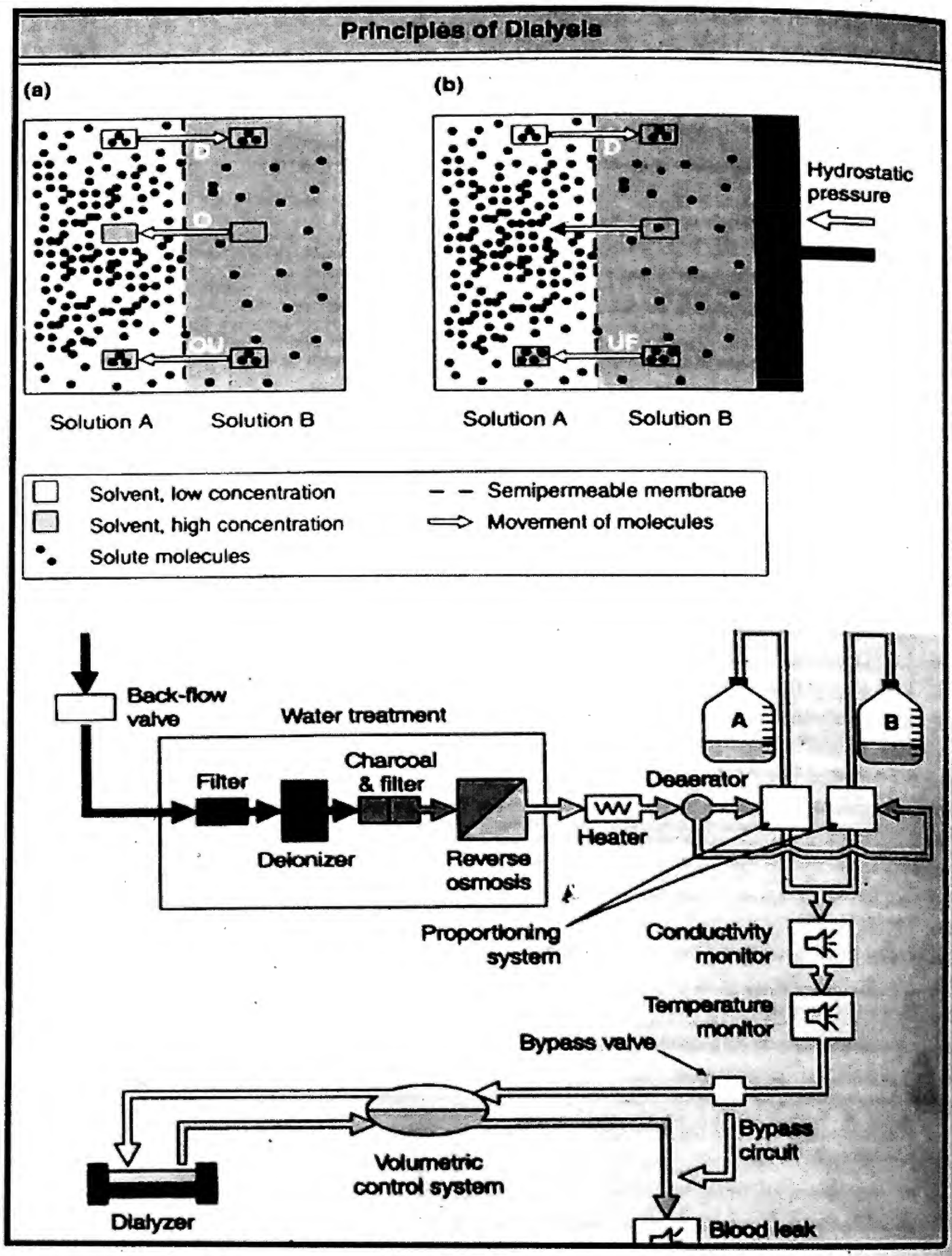
1. Complete Market and Feasibility Study.
2. Obtain Government approval
3. Obtain Finances
4. Decide whether to have in-patient only, out-patient only or both facilities
5. Acute dialysis units should preferably be located in the Emergency area of the hospital.

Steps in Design:

1. Selection of an Architect: Architect will provide assistance in determining the construction budget and space requirements for the facility and selecting site.
   Criteria for selection of the architect include excellence in design, technical competence and sound project management.
2. Establish space and Functional programme: A 20 station dialysis facility will usually require between 540 and 765 m² (6000 and 8500 ft²) of gross floor area or about 27 and 38.25 m²) per patient.
3. Land site: In choosing a land site, sufficient site area must be available to accommodate the parking required by zoning codes, as well as that actually needed. The site must provide delivery access for trucks as large as tractor trailers. An outside space should be provided for a trash dumpster.
4. Preparation of budgets of construction equipment and furnishing: Major built-in medical equipment, namely the central delivery system, dialysis machines and water treatment systems should be selected and orders placed for its purchase.
5. Upon approval of the final architectural design, the working drawings and specifications for construction are begun and contractor selected.
6. Interior design work should be undertaken at the same time.
7. After completion of construction: The following are undertaken:
   - Check out phase of contractors work.
   - Working the equipment and debugging.
   - Delivery and installation of furnishings and supplies.
   - Familiarizing staff with the facility.



1. Keep patient side clamp (A) on
   - Open clamps B and C
   - Let small volume of fluid flush the tubes
2. Close clamp B
   - Open clamp A
   - Drain all fluid from the patient into the empty bag
3. Close clamp C
   - Open clamp B and fill the peritoneal cavity



Various Specifications and Standards:

1. Location: Should be such that it is available for both in-patient and out-patient use.
2. Patient area:

a. Acute Dialysis Units: Individual cubicles separated by non-flammable cubicle curtains, fixed non-combustible dividing partitions or movable screens.

b. Bed Space: 150 sq.feet per bed.

c. Area: The maximum area of any multi-unit dialysis room shall not exceed 5000sq.feet.

d. Surgical-type scrub sinks fitted with other than hand controls should be provided for patient use (knee/elbow operated) in chronic dialysis units at a ration of one sink for 10 patients. Scrub sink may be omitted in acute dialysis units.

e. A patient toilet room with water closet and lavatory shall be provided in each unit.

f. Hand washing facilities for staff use with other than hand controls shall be provided in all units. No lavatory shall be located more than 25 feet from each bed or chair.

g. Every dialysis unit shall have the capability of providing special emergency services when needed including but not limited to heart defibrillation and shall include:
   - A defibrillator
   - Crash Cast
   - Oxygen and
   - Suction equipment.

h. Furnishing will include:
   - Over-bed table or other table
   - Adequate light for reading and monitoring of patient.
   - Nurses cell
   - Television, visible for all beds.

3. Services:
   a. Nursing station
   b. Toilet
   c. Clean work room large enough for all functions of the units along with clean linen storage area.
   d. Dirty utility room.
   e. Hopper sinks for small instruments.
   f. Washing, bagging and holding of soiled linen and facilities for bed-pan flushing.
   g. Facilities for sterilizing. This can be within the unit or centrally placed (located).
   h. Nourishing unit.
   i. Medi-prep area.
   j. Equipment storage room.
   k. Office space.
   l. Refrigeration for specimen storage.
4. Special Plumbing requirements:
   a. Water supply pipes to dialysis machines shall be sized larger than regular water supply pipes to ensure rapid water supply and replacement while machines are operating.
   b. At least one floor drain in eachr dialysis unit shall be provided.
   c. Water used for dialysis purpose is analyzed periodically and treated as necessary to maintain continuous water supply that is biologically and chemically compatible with acceptable dialysis-water standards.
   d. Water shall be treated, when necessary, to remove presence of any calcium and or fluorine in the institutional water supply.
5. Dietary Facilities Department:
   a. Food pantry is provided.
   b. Control station for receiving food supplies.
   c. Storage space for 4 days supply including food requiring cold storage.

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limited to patients who are ACE- inhibitors intolerant.

Beta - Adrenenegic Receptor- Blocking Agents

Administer to all NYHA Class II or III patients with systolic heart failure, often together with ACE inhibitors and diuretics.

Contraindications:

Bronchospastic disease

Symptomatic bradycardia or advanced heart block

Unstable heart failure

Trail name	Agent	NYHA Glass	12- MO Effect size(%)
CIBIS	Bisoprolol	III-IV	-20
Carvedilol U.S.	Carvedilol	II-III	-66
MERIT-HF	Metoprolol	II-IV	-35
BEST	Bucindolol	III-IV	

BEST = Beta-blocker Evaluation Survival Trial.

CIBIS = Cardiac Insufficiency Bisoprolol Study.

MERIT-HF = Metoprolol CR/XL Randomised Intervention Trail in Congestive Heart failure.

Beta- adrenenegic receptor - blocking agents are administered in all NYHA class II or III patients with systolic HF

Other Antiadrenergic Agents & Edothelin Antagonists

Miscellaneous antiadrenergic agents

Dopamine 3 - hydroxylase inhibitor-Nepicastat

Endothelia Antagonists

Endothelin-1, a peptide synthesized in endothelium; acts as an autocrine or paracrine substance; has powerful biological effects mediated through ETA and ETB.

In CCF RTA/ETB ratio increases from 60:40 to 80:20.

Nonselective and EAT selective antagonistic (trail stage) produce vasodilator effects with increase in cardiac output.

Bosentan is a nonselective antagonist.

TNF-Alpha Inhibitors

- TNF- Alpha production is induced in cardiac myocytes in failing heart.
- It causes cardiac myocyte hypertrophy leading to myocardial dysfunction.
- TNF-Alpha receptor inhibitor- etanercept is reported to improve left ventricular function.

Positive Inotropic Agents

- **Phosphodiestrase inhibitor**
  - Amrinone
  - Milrinone
  - Enoximone
  - Vesnarinone
- Phosphodiestrase inhibitor with calcium sensitizer Activity
  - Pimobendan
  - Levosimendan
  - Digoxin trail Results
  - Randomised Assessment of Digoxin and inhibitors Angiotensin-converting enzyme (RADIANCE).
  - Digoxin Investigation Group (DIG).

Above trials support the routine use of digoxin in patients in sinus rhythm with mild-moderate HF (NYHAII-III)> Digoxin is required in all HF patients with atrial fibrillation in whom ventricular response slowing is required.

Assisted Circulation

- **Selection Criteria**
- Hemodynamic criteria of cardiogenic shock
- Maximal inotropic support and intraaortic balloon counter pulsation
- **Exclude patient if**
- Blood urea nitrogen > 100mg/dl
- Serum Creatinine > 5 mg/dl
- Chronic lung disease
- Chronic liver disease
- Metastatic cancer
- Systemic sepsis
- Neurological deficit
- Technically incomplete cardiac operative procedure
- Age > 65 years

Assisted Circulation

Mechanical circulatory support devices can be divided in to three groups.

- IAB is a catheter mounted intravascular device designed to improve the balance between myocardial oxygen supply and demand with a modest increase in systemic perfusion.
- VAD is a blood pump designed to replace/assist the function of either ventricle.
- TAH is an orthotopically positioned cardiac replacement device.

Cardiac Transplantation

- **Indications**
  - End stage heart disease that limits prognosis for survival over 2year or several limits daily quality of life despite optimal medical and other surgical therapy.
  - No secondary exclusion criteria.
  - Suitable psychosocial profile and socials support system.
  - Suitable physiologic/ chronologic age.

Cardiac Transplantation

- Exclusion criteria
  - Active infectious process.
  - Recent pulmonary infarction.
  - Insulin - requiring diabetes with evidence of end- organ damage.
  - Irreversible pulmonary hypertension
  - Presence of circulation cytotoxic antibodies.
  - Active malignancy.
  - Presence of service C.O.P.D.
  - Substance of alcohol abuse.
  - Presence of peripheral or cerebrovascular disease.

Pacing for Heart Failure

Biventricular pacing/ left ventricular pacing may be beneficial in a subset of patient with intraventricular conduction delay. This is based on the strategy that subjects with intraventricular condition delay have asynchronous left ventricular contraction which results in a reduction in ventricular performance.

Biventricular pacing with defibrillator capability are treatment of choice in patients with left ventricular dysfunction who have survived sudden cardiac death, have symptomatic sustained ventricular tachycardia or have a symptomatic non-sustained but inducible ventricular tachycardia.

Important Clinical Signs in Dermatology

Imran Majid

INTRODUCTION

As in any other branch of medical science there are certain important and well-known clinical signs in field of dermatology. These signs go a long way in establishing a clinical diagnosis or else judge the severity of disease in an individual patient. Some of the most important ones among these are discussed here for the benefit of medical students.

1. Auspitz Sign

This clinical sign is seen in psoriasis.

On scrapping a lesion of psoriasis with a blunt glass slide silvery scales are observed followed by a glistening transparent membrane. On removal of this membrane [Buckley's membrane] multiple small bleeding point are observed.

The basis for this sign is a combination of suprapapillary thinning of the epidermis with dilatation of subpapillary dermal blood vessels.

The sign is absent in pustular psoriasis and inverse psoriasis.

2. Asboe-Hansen's Sign

This sign is seen in pemphigus.

On application of pressure at one end of a bulla in pemphigus the lesion [bulla] spreads away from the margin.

The basis for this sign is the loss of cohesion of epidermal keratinocytes leading to an easy seperation of upper layers of the epidermis from the basal layer.

3. Buerger's Sign

This is a diagnostic sign for lower limb ischemia due to arterial disease.

Elevation of the lower limb causes pallor, most evident on the soles while dependency leads to a delayed but exaggerated hyperemia of the limb, most pronounced on the dorsa of feet.

4. Carpet Tack Sign

This sign is diagnostic of Discoid Lupus Erythematosus [DLE].

Removal of an adherent scale from a lesion of DLE reveals the undersurface to be covered with horny plugs [resembling carpet tacks] overlying dilated hair follicular openings.

5. Crowe's Sign

This sign is a feature of Neurofibromatosis Type1.

There is a diffuse freckling of axillae in patients with Neurofibromatosis Type 1- known as Crowe's sign.

6. Darier's Sign

This sign is diagnostic of Cutaneous Mastocytosis.

Scrapping a pigmented macular lesion of urticaria pigmentosa [cutaneous mastocytosis] leads to local itching, erythema and wealing.

The sign is elicited due to release of histamine from the mast cells locally in lesional skin.

7. Dimple Sign [Fitzpatrick Sign]

This clinical sign is seen in Dermatofibroma.

If the overlying epidermis is squeezed over a lesion of dermatofibroma, a dimple is seen in the center.

The sign is due to tethering of overlying epidermis to the dermal lesion at the center.

8. Dubois Sign

This sign is one of the stigmata of Congenital Syphilis.

Denotes the presence of a very short little finger in a patient with Congenital Syphilis.

9. Flag Sign

This is seen in Kwashiorkor and other diseases leading to severe protein malnutrition like extensive bowel resection, severe ulcerative colitis etc.

Presence of alternating white and dark bands along individual hair shafts is known as flag sign. The bands are formed due to intermittent severe protein malnutrition.

10. Forschheimer's Sign

This sign is seen in Rubella and was originally described by Forschheimer.

The name is given to an enanthem [mucosal rash] that is confined to the soft palate during the prodromal period in Rubella.

11. Gottron's Sign

This sign is seen in Dermatomyositis.

There is a linear erythematous streaking over the dorsa of hands distributed over the extensor tendons. The sign is different from Gottron's papules, which are voilaceus or erythematous papules over the knuckles or dorsa of finger joints.

12. Groove Sign

This sign is seen in Lymphogranuloma venereum [LGV].

The sign has been originally described by Greenblatt.

Enlargement of inguinal lymph nodes above and femoral lymph nodes below the inguinal ligament gives a bubo of LGV a grooved appearance in the center.

13. Head-light Sign

This sign is seen in atopic eczema.

Perinasal and periorbital pallor is commonly seen in patients with atopic eczema and is known as head-light sign.

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14. Hertoghe's Sign

This sign is seen in atopic eczema as well as hypothyroidism.

The sign denotes the thinning of lateral part of eyebrows in these patients.

15. Higoumenakis Sign

This is pathognomic of Congenital Syphilis.

An irregular thickening or enlargement of the sternal end of clavicle, usually unilateral is given the name of Higoumenakis sign.

16. Hutchinson Sign

This is the name given to at least two different clinical signs in two different disease entities.

A, In Subungual melanoma

Presence of a longitudinal melanotic streak on the nail plate accompanied by periungual pigmentation is diagnostic of a subungual melanoma and is called Hutchinson's sign.

B, In Ophthalmic Herpes Zoster

Appearance of vesicles on the tip or dorsum of nose is indicative of the involvement of the Nasociliary nerve and thus predicts the involvement of eye in Ophthalmic nerve zoster. This is also given the name of Hutchinson's sign.

17. Sign Of Lesser Trelat

Sudden appearance of numerous seborrheic keratoses on the body with/without pruritus is taken as a marker for the presence of an internal malignancy and is known as the Sign of Lesser Trelat.

18. Nikolsky's Sign

This sign is seen in Pemphigus, Toxic Epidermal Necrolysis [TEN], Staphylococcal Scalded Skin Syndrome [SSSS] and also in burns.

The sign denotes the removal of epidermis as a sheet on application of a tangential pressure over normal skin near a bullous lesion, preferably over a bony prominence.

The basis for the sign is the loss of normal cohesion of epidermal keratinocytes in the above-mentioned conditions.

19. Nose Sign

This sign is seen in erythroderma of atopic origin.

When erythroderma [>90% body surface area involvement] occurs in a patient of atopic eczema the nose and perinasal area are characteristically spared in presence of involvement of other areas of face. This is called nose sign.

20. Oil Drop Sign

This sign is seen in psoriasis of nails.

Circular areas of discoloration of nail bed and hyponychium occur as a result of involvement of these structures in psoriasis. As these areas resemble oil drops below the nail, hence the name of oil-drop sign.

21. Olendroff's Sign

This sign is seen in secondary syphilis.

Individual papules of a papular or papulosquamous syphilid are exquisitely tender to the touch of a blunt probe.

22. Orentreich Sign

This is seen in Trichotillomania.

In severe forms of the disease, when the whole scalp is involved the hair at the margins is characteristically spared. This is known as Orentreich sign or Tonsure alopecia. The sign has also been described under the name of 'Friar-Tuck sign'.

23. Osler's Sign

This is seen in Alkaptonuria.

Deposition of pigment becomes apparent by third decade of life and the first organ where this pigmentation is apparent to the naked eye is the sclera of eyes. This scleral pigmentation is known as Osler's sign.

24. Thinker's Sign

This sign is seen in COPD.

Due to a characteristic dyspnoeic posture assumed by COPD patients, asymptomatic dry and hyperpigmented keratotic plaques develop over time on the front of the lower third of thighs. Presence of these plaques in patients with COPD is known as Thinker's sign.

25. Tongue Sign Of Uraemia

This sign has been described by M. Thomas Mathew.

Large pale tongue with prominent impression of teeth all around the edges is a charactersistic feature of uraemia and is known as Tongue sign of uraemia.

26. Wimberger's Sign

This clinical sign is seen in Congenital Syphilis.

An X-ray of the tibia shows loss of density on the medial side of its upper end.

MRI-A Cost Effective Technology

Waseem Qureshi, Majid Jehangir, Khursheed Qureshi, Ghulam Hassan, Abdul Majid, S.M. Kadiri

Imaging technology has undergone a tremendous progress from Roentgen's discovery of X-rays to present day Ultrasound (USG) Computed Tomography (CT) and Magnetic resonance imaging (MRI). MRI was introduced into clinical medicine in 1981 been hailed as the most exciting-event in medical imaging [1].

Initially used for diagnosing disorders of central nervous system and musculoskeletal system, use of NRI in neck, heart, mediastinum and abdomen is rapidly increasing. MR Angiography, MR Cholangiopancreatography, MR Spectroscopy and Functional MRI are gaining clinical importance.

MRI is unquestionably the imaging modality of choice for disorders of central nervous system. In a study by Bradley et al [2] comparing CT & MRI evaluation of 400 patients with suspected disease in brain and cervical cord. MRI demonstrated abnormalities in 30% of cases in which CT done earlier had beer entirely normal.

Although the diagnostic efficacy of MRI is generally accepted, this expensive imaging modality has lead to substantial increase in health care costs- In this perspective two types of comparisons are possible. Comparing the costs involved in obtaining the diagnosis is know as "Cost Benefit Analysis" [4].The other type of comparison that focuses on quality of life is known as "Cost Effective Analysis" [5]. In such a Comparison MRI is more efficacious by providing early diagnosis which in turn may allow less radical surgery in patients such as having intracranial space occupying lesions. MRI even if reported normal may improve the quality of life by excluding a suspected disorder with high specificity and sensitivity.

In "Cost Benefit Analysis" the cost of MRI is compared with the cost of investigations from providing the same diagnosis without MRI. Moreover the comparison is based on "indication for MRI" rather than the final predicated diagnosis. A study of this type by Bradley, Stuart and Kortman compared the technical charges for evaluating the patient by MRI with the charges that would have been incurred had the patients been evaluated by traditional methods of imaging in the study saving of. 25% was shown for the patients having MRI. The maximum saving was achieved when MRI was done out patient basis and infact it has replaced Myelography which is being done only after hospitalization the patients.

However, in a recent study by Javik J G et al [6] determining the clinical and economic consequences of replacing spine radiographs with rapid MRI in patients of low backache, MRI was found to be costlier than radiographs but can be cheaper if cost of unnecessary operations are excluded. In another study by Jager G J et al [7] pre-operative MRI staying of CA prostate. MRI was found to reduce the costs and resulted in almost equal life expectancy and quality adjusted life years.

Bradley [8] assessed the financial viability of an MRI unit after 27 months of its operation in their institute, during which period 5000 patients were studied. When expenses were compared to revenue actually collected during the fiscal year and there was a profit of 6.3%.

Thus, these studies do provide the evidence that MRI is cost effective however this needs to be considered case by case and as per compelling indication.

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Anticoagulation Theray- Newer Insights

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Arterial and venous thrombosis are major causes of morbidity and mortality in medical practice. Arterial thrombosis is the commonest cause of Myocardial infarction, strokes and sometimes limb gangrene whereas venous thrombosis can lead to pulmonary embolism a potentially fatal condition. Because arterial thrombi consist mainly of platelet aggregates held together by small amounts of fibrin, strategies to inhibit arterial thrombogenesis focus mainly on durgs blocking platelet function but also include anticoagulant agents to prevent fibrin deposition. In contrast, venous thrombi are composed mainly of fibrin, anti coagulants are the main drugs for their prevention and treatment. Anti coagulants are also used for prevention of cardioembolic events in patients with atrial fibrillation and mechanical heart valves.

Before discussing the various anti coagulants (older as well as novel agents) it is necessary to understand the basics of thrombogenesis including its initiation, propagation as well as its regulation.

Thrombogenesis

Arterial thrombosis usually is initiated by the rupture of atherosclerotic plaque, a process that exposes thrombogenic material in the lipid rich core of the plaque to blood [1]. The thrombi that form at sites of plaque disruption extend both into the plaque as well as the vessel lumen. With more extensive intraluminal thrombosis blood flow diminishes and shear increases which promotes further platelet and fibrin deposition that may result in the formation of an occlusive thrombus which obstructs blood flow to the target organ.

Venous thrombosis (composed mainly of fibrin and RBC's) occurs when procoagulant stimuli overwhelm natural anticoagulant mechanisms. Procoagulant stimuli include the excessive activation of coagulation particularly when protective pathways are compromised by thrombophilic abnormalities, vessel wall damage or stasis. Patients with congenital deficiency of antithrombin,, protein C, protein S as well as patients with factor V Leiden mutation (protein C resistance) are prone to thrombosis because naturally occurring anti coagulant pathways are compromised. Venous thrombi develop under low flow conditions and usually originate in the muscular venis of the calf or in the valve cusp pockets of the deep calf veins [2]. As venous valve cusps are avascular they depend on the circulating blood for their oxygen and nutrient supply. With stasis there is hypoxia which can induce tissue factor expression in the valve cusps. Coagulation in the veins can also be initiated by trauma. Damage to the vessel wall is a particularly important predisposing factor to venous thrombosis after major hip or knee surgery. Indwelling central venous catheters also can injure the vein wall, causing DVT in the upper extranity.

The initiation of coagulation in vessels is triggered by tissue factor, a cellular receptor for activated factor VII [3]. Injury to the arterial or venous wall exposes nonvascular, tissue factor expressing cells to blood. Lipid laden macrophages in the core of atherosclerotic plaques are particularly rich in tissue factor, thereby explaining the propensity for thrombus formation at sites of plaque disruption. Once bound to tissue factor, factor VIIa activates factor IX and factor X leading to the generation of activated factor IX (IXa) and activated factor X (factor Xa) respectively. Factor X activation is more efficient than factor IX activation. Factor Xa converts small amounts of prothrombin to thrombin. This low concentration of thrombin is sufficient to activate platelets and to activate factor V and VIII which are key cofactors in coagulation. These thrombin mediated steps are essential for the propogation of coagulation.

The propogation of coagulation is effected by factors IXa and Xa. In the presence of Ca, factor IXa bind to factors VIIIa on the surface of activated platelets to form intrinsic tenase, the complex that activates factor X. Factor Xa then binds to factor Va on the activated platelet surface, a process that is also Ca dependant, to form prothrombinase complex. This complex activates prothrombin and the resultant thrombin then dissociates from the platelet surface and converts fibrinogen to fibrin monomer. Fibrin monomers polymerize to form the fibrin mesh that is stabilized and cross linked by activated factor XIII, a thrombin activated transglutaminase. Thrombin amplifies its own generation by the feed back activation of factor V and factor VII and by activating platelet bound factor XI thereby leading to further factor Xa generation [4].

Regulation of Coagulation

Coagulation is regulated at several levels. Key inhibitors include tissue

factor pathway inhihitor (TFPI), antithrombin and protein C pathway.

Another important regulating system is the fibrinolytic system itself. Fibrinolytic system serves to degrade fibrin once it has served its role in haemostasis.

As many newer anti coagulant strategies are aimed at enhancing endogenous anti coagulant or fibrinolytic mechanisms. It is relevant to have a brief review of these pathways.

TFPI: The inhibition of factor VII a /tissue factor complex is effected by TFPI [5], which is a bivalent inhibitor and acts in a two step manner. In the first step, TFPI complexes and inactivates factor Xa to form a TFPI/Factor Xa complex. The TFPI within this complex then inactivates tissue factor bound factor VIIa as the second step. Because the formation of TFPI/Factor Xa complex is a pre requisite for the efficient inactivation of factor VIIa, the system ensures that some factor Xa generation occurs before factor VIIa mediated initiation of the coagulation system is shut down. However, the propogation of coagulation occurs because TFPI concentration are low. In addition, factor XI which is efficiently activated by thrombin when bound to activated platelet surface generates factor IXa. A key component of the intrinsic tenase complex, factor IX a triggers the formation of sufficient amounts of factor Xa to propagate coagulation.

Most circulating TFPI is bound to lipoproteins, also found in platelet x-granules and on the endothelial cell surface. TFPI bound to the endothelium is released with therapeutic doses of heparins. It is uncertain, however, whether released TFPI contributes to the antithrombotic properties of these agents.

Anitthrombin

Antrithrombin inhibits thrombin, factor Xa and other activated clotting factors, but these reactions are slow in the absence of heparin. With heparin, the rate of inhibition is accelerated about 1000 folds [6]. Heparin binds to antithrombin via its high affinity pentasaccharide sequence and by altering the conformation of the reactive centre loop of antithrombin renders the protease trap more accessible to target enzymes.

Protein C pathway:

In addition to antithrombin, thrombin also is inhibited by binding to thrombomdulin, a thrombin receptor found on the endothelium. Once bound thrombin undergoes conformational change at its active site that converts it from a procoagulant enzyme into a potent activator of protein C (a vit. K dependant protein). Activated protein C serves as an anticoagulant by proteolytically degrading and inactivating factors Va and VIIIa thereby attenuating thrombin generation.[7] This reaction occurs on negatively charged phospholipids surfaces where protein S , another vit. K dependant protein, serves as a cofactor.

Fibrinolytic system:

Designed to remove intravascular fibrin thereby restoring blood flow, fibrinolysis is initiated by plasminogen activators that convert plasminogen to plasmin. A trypsin like protease, plasmin degrades fibrin into soluble fibrin degradation products. Two plasminogen activators are found in blood, tissue-type plasminogen activator (tPA), and urokinase-type plasminogen activator (UPA). Both of them are synthesized and released from endothelial cells[8]. Intravascular plasminogen activation is initiated by tPA. Plasminogen activation is targeted to fibrin because plasminogen and tPA is enhanced by fibrin. protease that links fibrinolysis with coagulation has been identified. Known as factor VII activating protease (FSAP), this protease not only activates factor VII, as its name implies, but also converts single chain UPA (prourokinase) into the active two chain form[9].

The fibrinolytic system is regulated at two levels. Plasminogen activator inhibitors, the most important of which is endothelial cell-derived type I plasminogen activator inlhibitor (PAI-1), block tPA whereas ∝2- antiplasmin inhibits plasmin. Although ∝2-antiplasmin rapidly complexes and inactivates free plasmin, fibrin bound plasmin is relatively protected from inactivation so that fibrinolysis can occur despite physiological levels of this inhibitor.

A procarboxypeptidase B that serves as a link between coagulation and fibrinolysis has been identified in plasma. Activated by the thrombin/thrombomodulin complexes, this enzyme known as thrombin activable fibrinolysis inhibitor (TAFI), attenuates fibrinolysis by clearing carboxyl-terminal lysine residues from fibrin [10]. The removal of these lysine residues decreases plasminogen and plasmin binding to fibrin, thereby retarding the lytic process.

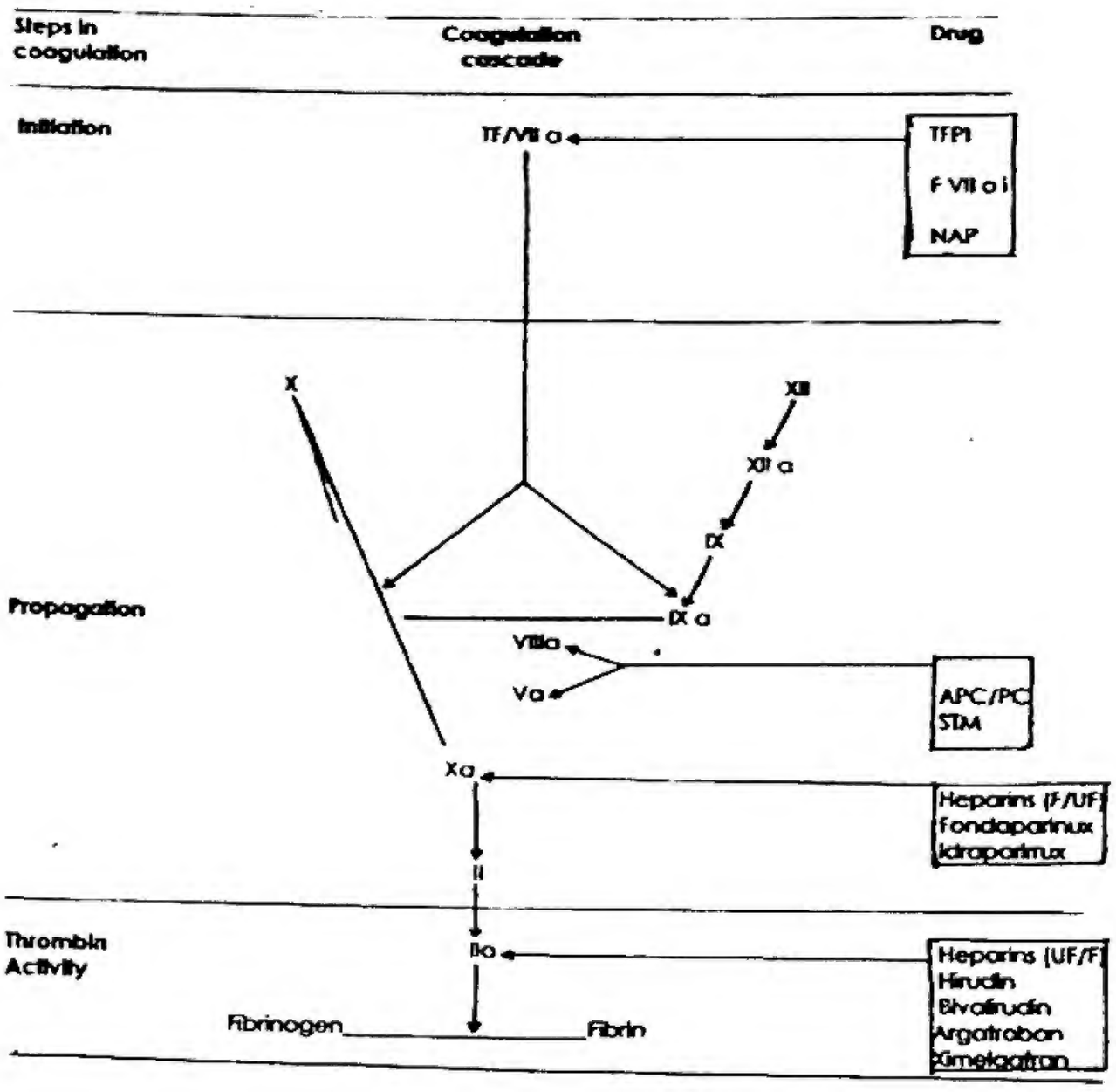
Development of newer anticoagulants:

Better understanding of the molecular mechanisms underlying blood coagulation, recombinant DNA technology, isolation and characterization of anti coagulant proteins from blood sucking organisms have accelerated the pace of drug discovery and now an array of newer anticoagulants targeting specific clloting enzymes or steps in coagulation are available and are being tested in clinical trials.

A. Inhibitors of initiation of Coagulation:

Drugs that target the factor VIIa/tissue factor complex inhibit the initiation of coagulation. Agents in this category that have reached phase II clinical testing include recombinant TFPI, recombinant nematode anticoagulant peptide (NAPC2) and

STEPS IN BLOOD COAGULATION



TF: Tissue factor: TFPI: Tissue factor pathway inhibitor: F VII ai; factor VII activated inhibitor: APC: activated protein C: PC: Protein C: STM: Soluble thrombomodulin.

inhibitor of factor VIIa (factor VIIa i).

1.TFPI: Synthesized by recombinant technology tifacogin is being evaluated in patients with sepsis syndromes and other thromboprophylaxis situations [11].

2. NAPC2: An 85 aminoacid polypeptide was originally isolated from canine hookworm Ancylostoma caninum. It binds to a non-catalytic site on factor X or factor Xa. Once bound this factor complex inhibits factor VIIa bound to tissue factor. Because it binds to factor X with high affinity NAPC2 has a half life of approximately 50 hrs after subcutaneous injection. Clinical trials are underway evaluating NAPC2 for thromboprophylaxis after knee surgeries as well as arterial thrombosis for unstable angina, Non-ST elevation MI, and those undergoing PCI.

3. FactorVIIai: By competing with factor VIIa for tissue factor binding, factor VIIai attenuates the initiation of coagulation by the factor VIIa/tissue factor complex. Based on promising results in animal models of thrombosis, treatment with factor VIIai in doses renging from 50 to 400 mg/kg with or without adjunctive heparin was compared with heparin alone in patients undergoing elective PCI [11]. However, the results were disappointing and thus factor VIIai has not been developed further.

B. Inhibitors of propagation of Coagulation:

Drugs blocking factor IXa, factor Xa or their cofactors, VIIIa and Va inhibit propogation of coagulation. Factor IXa inhibitors have not yet reached clinical trials.

Factor Xa inhibitors include agents that block factor Xa directly or indirectly. Indirect inhibitors act by catalyzing factor Xa inhibition by anti thrombin; while direct inhibitors bind directly to the active site of factor Xa, thereby blocking its interaction with its substrates. Unlike the heparin/antithrombin complex, direct factor Xa inhibitors not only inhibit free factor Xa but also inactivate platelet bound factor Xa within prothrombinase complex.

Fondaparinux and Idraparinux atre two new parental indirect factor Xa inhibitors. A new orally active direct factor Xa inhibitor DPC 906 is under active clinical research.

Inhibition of factor Va and VIIIa is effected by activated protein C, which thus can be achieved by directly administering recombinant activated protein C or its precursor, protein C. Recombinant soluble thrombomodulin, another means of generating activated protein C, also is under evaluation.

Fondaparinux

It is a synthetic analog of antithrombin binding pentasaccharide sequence found in heparins (UFH/LMWH). Fondaparinux binds antithrombin and enhances its reactivity with factor Xa. Because it is too short to bridge antithrombin to thrombin, fondaparinux has no activity against thrombin.

Because of its excellent bioavailability after subcutaneous injection and a plasma half life of about 17 hrs. Fondaparinux can be administered subcutaneously once daily. The drug is excreted unchanged in urine hence dosage adjustments are necessary in patients with renal insufficiency and is contraindicated in renal failure.

It does not bind to platelets or platelet factor 4 (PF4). As it does not induce the formation of heparin/PF4 complexes that serve as antigenic target for the antibodies that cause heparin-induced thrombocytopenia (HIT), HIT is unlikely to occur with fondaparinux. Fondaparinux also fails to interact with protamine sulfate, the antidote for heparin. If uncontrolled bleeding occurs with fondaparinux, a procoagulant such as recombinant factor VIIa might be effective, however, the latter is expensive, not freely available and can cause thrombotic complications.

Fondaparinux has been evaluated for the prevention and treatment of venous thromboembolism as well as for the treatment of arterial thrombosis.

For venous thromboprophylaxis it has been evaluated in patients undergoing major orthopaedic surgery, in general medical and surgical patients. Based on many large trials comparing fondaparinux with enoxaparin for thromboprophylaxis in patients undergoing surgery for hip fracture or elective hip or knee arthroplasty, Fondaparinux has been licensed for this indication [14] and in these trials it was found to reduce the risk of venous thromboembolism by approximately 55 % compared to enoxaparin.

For the treatment of venous thromboembolism fondaparinux was compared with enoxaparin in two trials, MATISSE DVT trial[15] and MATISSE PE trial [16] and it was found to be at least as effective and safe as LMWH or UFH.

For the treatment of acute coronary syndromes fondaparinux has been evaluated in phase II clinical trials in evolving ST elevation MI (to receive fondaparinux in various doses or UFH as adjuncts to alteplase and aspirin) and also in unstable angina/ NSTEMI (comparing subcutaneous fondaparinux 2.5- 12 mg daily to enoxaparin 1 mg/kg twice daily)[17]. In all these trials the results were encouraging, however, the lack of a dose response with fondaparinux therapy in phase II trials makes it difficult to identify the optimal dose. Consequently additional dose-finding studies may be necessary before undertaking a large scale phase III clinical trials.

Idraparinux

It is a highly sulfated derivative of fondaparinux and binds antithrombin with such a high affinity that its plasma half life of 130 hrs. is similar to that of antithrombin. Because of its long half life, idraparinux can be given once weekly. Because of its such a long half life bleeding chances are more which can be difficult to control. Trials[18] comparing 10 mg, 7.5 mg and 5 mg wkly doses of idraparinux with warfarin have shown severe bleeding tendencies with these doses. Hence at present once weekly 2.5 mg dose of idraparinux is being compared in phase III clinical trials.

Activated protein C

Recombinant activated protein C, drotrecogin alfa has been compared in clinical trials with placebo and was found effective. Based on these trials the drug has been licensed for use in North America for the treatment of patients with severe sepsis [19].

Protein C:

Promising results have been reported in patients with meningococcemia. For theoretical reasons activated protein C may be a better choice than protein C in patients with severe sepsis because inflaminatory cytokines down regulate thrombomodulin expression on the endothelial surface.

Soluble thrombomodulin:

A recombinant analog of thrombomodulin, soluble thrombomodulin binds thrombin and induces a conformational change in the active site of the enzyme that converts it into a potent activated of protein C. Presently the drug is undergoing clinical trials.

C.Inhibitors of fibrin formation:

Thrombin the enzyme that converts fibrinogen to fibrin, can be inhibited indirectly or directly. Indirect inhibitors act by catalyzing antithrombin. In contrast direct inhibitors bind directly to thrombin and block its interaction with substrates.

Direct thrombin inhibitors have properties that give them potential advantages over indirect thrombin inhibitors such as heparin. First, because direct thrombin inhibitors do not bind plasma proteins, they produce a more predictable anticoagulant response. Second, unlike heparin, direct thrombin inhibitors do not bind to PF4. Consequently the anticoagulant activity of these drugs is unaffected by large quantities of PF4 released in the vicinity of platelet rich thrombi and thrombocytopenia is not seen with these drugs. Finally direct thrombin inhibitors inactivate fibrin-bound thrombin, as well as free thrombin.

There direct thrombin inhibitors (Hirudin, bivalirudin, argatroban) have been licensed in North America for various

indications and are also approved for the treatment in patients with Heparin induced thrombocytopenia.

Ximelgatran, a prodrug of melagatran is the first orally available direct thrombin inhibitor.

Hirudin

Originally isolated from the saliva of medicinal leech Hirudo medicinalis it consists of 65 amino acid polypeptide and is now available in recombinant form[20]. The hirudin/thrombin complex is essentially irreversible a potential drawback as there is no specific antidote. The plasma half life of hirudin is 60 mts after IV injection and 120 mts after sub cutaneous injection. It is cleared via the kidneys and is contraindicated in patients with renal failure[21]. The anticoagulant effect of Hirudin can be monitored by APTT.

Recombinant Hirudin (lepirudin) is licensed for the treatment of arterial or venousthrombosis complicating HIT. It has been evaluated in acute coronary syndromes as well as for the prevention and treatment of venous thrombosis.

In unstable angina it was evaluated in trials like Organization to Assess Strategies for Ischemic Syndromes (OASIS)- 1 & 2 [22,23], where it was found to be at least as effective as heparin but there was tendency towards an increase in major bleeding episodes with Hirudin.

In patients with Myocardial infarction it was evaluated as an adjunct to thrombolytic therapy and compared with Heparin in three trials. TIMI-9A[24], Hirudin for improvement of thrombolysis (HIT)-III [25] and Global use of Strategies to open Occluded Coronary arteries (GUSTO)-II A [26]. All three trials were stopped prematurely because of unacceptably high rates of major haemorrhage. Consequently GUSTO-IIA and TIMI 9A trials were re-started as the GUSTO-IIB [27] and TIMI-9B [28] trials using lower doses of hirudin than that used in GUSTO-I trial. In addition the dose of Heparin also was reduced to more closely match that used in the GUSTO I trial. Taken together, both the trials suggest that Hirudin therapy is at least as effective as heparin therapy when used as an adjunct to thrombolytic therapy.

In coronary angioplasty hirudin therapy was compared with heparin for the prevention of re stenosis after PCI in a trial named as HELVETICA study (Hirudin in a European trial versus Heparin in the Prevention of Restenosis After PTCA)[29]. Event free survival was similar in those receiving heparin, IV hirudin, or IV hirudin followed by subcutaneous hirudin. Likewise on repeat angiography at 6 month there was no significant difference in the mean luminal diameter of the dilated vessel among the three groups. No excess bleeding was seen with hirudin.

In venous thromboprophylaxis: Hirudin has been compared with unfractionated heparin and LMW Heparin for thromboprophylaxis in patients undergoing elective hip arthroplasty in two studies by Eriksson and Colleagues [30,31]. In both these studies hirudin therapy appeared to be more effective than unfractionated Heparin or LMWH for thromboprophylaxis after hip arthroplasty. Despite these findings, however, hirudin has not been approved for this indication.

For treatment of venous thromboembolism hirudin was compared with UFH in one study by Schiele et al [32]. Hirudin was found to be significantly more effective while major bleeding occurred in patients receiving the highest dose of hirudin and in those receiving UFH, occurring in 3 % patients in both groups.

Although hirudin appears promising for the prevention and treatment of venous thrombosis, the clinical development of the drug for these indications has not been pursued.

Bivalirudin (Hirulog)

It is a 20 amino acid synthetic polypeptide and an analog of hirudin. Like Hirudin it forms a 1:1 complex with thrombin. However, the complex formed is not irreversible like that of hirudin-thrombin, which makes bivalirudin safer than hirudin. It has a half life of 25 mts after I.V injection and only a fraction is excreted via the kidneys. Bivalirudin has been evaluated in patients undergoing percutaneous coronary intervention in trials like REPLACE-2 (Randomized Evaluation of PCI linking Angiomax to Reduced clinical Events) [33] which compared bivalirudin with GPIIb/IIIa antagonist (abciximab and Eptifibatide) and Heparin. It was also evaluated as an adjunct to thrombolysis in HERO-2 trial (Hirulog and Early reprefusion or OccInsion-2) [34] where it was compared with Heparin in ST elevation MI patients receiving streptokinase. Summarizing the results, Bivalirudin was found to be at least as effective as Heparin in patients undergoing PCI with less bleeding chances. For patients with low to moderate risk of bleeding who are undergoing PCI without receiving an adjunctive GPIIb/IIIa antagonist bivalirudin may be a better choice than heparin. As an adjunct to thrombolysis bivalirudin was found to reduce the risk of reinfarction as compared to heparin. However, bivalirudin requires monitoring and dose adjustment may be necessary to reduce the risk of bleeding.

Argatroban

Is a competitive inhibitor of thrombin forming a reversible complex with it. Has a half life of 45 mts and metabolized in liver thus to be used with caution in patients with hepatic dysfunction. Argatroban is the drug of choice for patients with HIT. In many small studies it has been evaluated in patients with unstable angina, as an adjunct to thrombolysis, as an alternative to heparin in patients undergoing coronary angioplasty but none has shown definitive advantage of argatroban over heparin.

Ximelagatran

Ximelagatran is a prodrug and after absorption in small intestine undergoes rapid biotransformation to melagatran. Ximalagatran has a plasma half life of 3-4 hrs and is administered orally twice daily. It produces a predictable anticoagulation response thus coagulation monitoring is unnecessary. Melagatran, the active agent is eliminated renally thus dose adjustments may be needed in elderly and in renal insufficiency. Ximelagatran is being evaluated in various studies for various indications as described below.

For venous thromboprophylaxis ximelagatran has been evaluated without or in combination with melagatran in studies like Melagatran for Thrombin Inhibition in Orthopaedic surgery II study [35] and another large one named as EXPRESS study [36]. The data available to date suggest that (a) the combination therapy of subcutaneous melagatran started prior to surgery followed by oral ximelagatran postoperatively is more effective than enoxaparin therapy for thromboprophylaxis after hip or knee arthroplasty but may cause more bleeding . (b) Postoperatively is likely to be at least as effective as warfarin for prophylaxis after knee arthroplasty. Unlike warfarin, however, ximalagatran does not require coagulation monitoring and thus may be useful for extended out of hospital prophylaxis in high risk patients.

For treatment of venous thrombosis ximelagatran was evaluated in various trials as Thrombin Inhibition in Venous Thromboembolism (THRIVE) I,II,III [37-39] where it was compared with low molecular weight heparin (followed by warfarin). These studies suggested that oral ximelagatran is as effective and safe as conventional anti coagulation (LMWH followed by warfarin) with advantage of ximelagatran being more convenient as it does not need monitoring.

Atrial fibrillation is one of the conditions where it has been studied with enthusiasm. Ximelagatran has been studied extensively in non-valvular atrial fibrillation in various SPORTIF (Stroke Prevention using Oral Thrombin Inhibition in Atrial Fibrillation) trials.

In SPORTIF II [40] patients were randomized to one of the three doses of ximalagatran (20,40 or 60 mg twice daily) or warfarin targeted to INR 2.0 to 3.0. At 12 weeks fewer patients in ximalagatran group had experienced TIA's (0.5% and 3% respectively) and one patient in ximalagatran group had an

Ischemic stroke compared with none in the warfarin group. There were no major incidents of bleeding in any patient in ximalagatran groups, but one major incident of non-intracranial bleeding was observed in a patient receiving warfarin. The SPORTIF IV [41] is an open label continuation of this trial comparing fixed dose of unmonitored ximalagatran (36 mg twice daily) with warfarin therapy.

SPORTIF III [42] used an open label design and was conducted in Europe , whereas SPORTIF V [43] is a blinded trial conducted in North America. The trials enrolled patients with non-valvular atrial fibrillation and at least one additional risk factor for stroke. When the results of SPORTIF III and SPORTIF V trials are combined, the absolute difference in the rate of stroke and systemic embolic events is 0.03 % lower in ximelagatran group, a difference that is not significant. The rates of major bleeding incidents with ximelagatran and warfarin therapy are 1.9 % and 2.5 % respectively. Thus these studies indicate that unmonitored ximelagatran therapy is a s effective and safe as dose adjusted warfarin therapy.

For the treatment of Myocardial infarction, ximelagatran in combnination with Aspirin was compared with placebo in patients who had experienced STEMI or NSTEMI in past 14 days in a phase II trial named as ESTEEM (Efficacy and Safety of the Oral Thrombin Inhibitor ximelagatran in combination with Aspirin, in patients with recent Myocardial Damage) [44]. The results were encouraging and thus a phase III trial is under consideration.

The most important side effect of ximelagatran is hepatotoxicity. Overall approximately 4 to 10 % of patients who receive long term treatment with ximelagatran develop an increase in alanine aminotraneferease levels. Typically occurs after 6 weeks to 4 months of treatment, is usually asymptomatic and reversible even if the medication is continued . In THRIVE trial however, one patient died of hepatorenal failure and from two other trials 2 patients died from Hepatic failure. This has contributed to the decision of the FDA to reject an initial application for approval of ximalagatran for prophylactic and treatment indication.

Reversal of anti coagulant effect of ximelagatran

In the event of acute bleeding the ability to promptly reverse the anticoagulant effect is a desirable property in any anti thrombotic agent. Both ximelagatran and fondaparinux at present lack a proven antidote. The ability of recombinant factor VIIa (rFVIIa) to normalize melagatran induced thrombin generation has been examined in a placebo controlled trial involving healthy male volunteers [45]. A single dose of rF VIIa of 90 mg /kg did not reverse the anticoagulant effects of melagatran as measured by endogenous thrombin potential. It was suggested that the role of repeated doses of continous infusion of FVIIa for this indication required further investigation.

Other direct thrombin inhibitors

Dabigatran is a low molecular weight direct thrombin inhibitor, administered orally as a prodrug dabigatran etexilate.

Efegatran is another direct thrombin inhibitor in this class.

D. Modulation of endogenous fibrinolytic activity

A better understanding of physiology of fibrinolysis has identified methods to enhance endogenous fibrinolytic activity. These include inhibitors of PAI-1, activated TAFI (TAFIa) or factor XIII a . Although the drugs are in early stage of development still some discussion about them is worthwhile.

A. PAI-1 Inhibitors:

PAI is a major physiological inhibitor of tPa and uPa, hence its inhibition results in increased endogenous fibrinolytic activity. PAI-1 activity can be reduced either by decreasing PAI-1 gene expression or by rducing the activity of PAI-1. Lipid lowering drugs Niacin and Fibrates decrease PAI-1 synthesis in vitro but they are not specific for PAI-1 and also affect synthesis of other proteins. Peptides have been identified that block PAI-1 activity but have yet to be tested in Vivo . More promising are small molecule PAI-1 inhibitors some of which exhibit antithrombotic activity in vivo.[46]

b. TAFIa inhibitors:

TAFIa attenuates fibrinolysis by cleaving carboxy-terminal lysine residues from fibrin, the removal of these lysine rebidues decreases plasminogen or plasmin binding to fibrin , thereby retarding the lytic process. A potato derived TAFIa inhibitor has been seen to increase plasminogen activator–induced thrombolysis in dogs and rabbits [47]. These observations have prompted the development of small molecule TAFIa inhibitors. A potential limitation of some agents is the paradoxical enhancement of TAFIa activity at low doses, probably reflecting allosteric modulation at the active site of the enzyme . If this phenomenon is common to all TAFIa inhiobitors, the optimal dosing of these agents will be problematic.

C.Factor XIIIa inhiobitors:

Factor XIIIa has the property of stabilizing the fibrin polymer by crosslinking its X-polymers and X-dimers thus rendering it more refractory to degradation by plasmin. The inhibition of factor XIIIa, therefore, has the potential to increase the susceptibility of thrombus to lysis.

Tridegin, a peptide isolated from the giant Amazon leech Haemanteria ghilianti, is a specific inhibitor of factor XIIIa and enhances fibrinolysis in vitro when added before cloting of fibrinogen [48]. Destabilase, a leech enzyme that hydrolyzes crosslinks also provides a promising approach to reversing the consequences of factor XIIIa-mediated fibrin crosslinking. None of these agents has yet been tested in humans.

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Vitiligo : What is New

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INTRODUCTION

Vitiligo is one of the oldest and also one of the commonest skin disorders affecting the human race. About 1-2% of the world population without any regard to the ethnic, racial or socioeconomic background suffers from this commonly recognized disorder[1]. The cosmetic impact of this disease is tremendous and its psychological impact devastating especially in dark races[2]. However, in spite of all these facts our understanding of this common disorder is still far from satisfactory. What do we know about this disorder now that we did not know a decade earlier? How far and how satisfactorily are we able to treat this disorder now? What are the new treatment options available for this disorder now that were not there a few years back and how far have they helped a dermatologist to cure this disorder? These are some of the questions that will be addressed in this paper!

NEW INSIGHTS INTO THE PATHOGENESIS OF VITILIGO

The etiology of vitiligo is still a debatable issue and the best that we can say about this matter at present is that we are still not absolutely certain about the pathogenesis of this disease. While we have gained new insights over the last decade or so into how this disease really occurs, we are still far away from the goal. All the classical theories for etiopathogenesis of vitiligo viz. the autoimmune theory; the neural hypothesis and the autocytotoxic theory are still in vogue and each one of them has its own proponents and supporters. However the theory that has gained the maximum support over the last few years is the 'Autoimmune theory'. Substantial data has accumulated from clinical research in recent times to implicate the 'faulty' immune system in the etiopathogenesis of vitiligo[3,4]. Many humoral as well as cell-mediated immune aberrations have been observed in patients with vitiligo.

On the humoral front specific autoantibodies have been observed with increased frequency in vitiligo patients[5,6]. These include antibodies against thyroglobulin, thyroid microsomes and thyroid peroxidase with respect to thyroid gland; gastric parietal cell antibodies and also antinuclear antibodies. In addition cytotoxic antibodies against both surface as well as cytoplasmic melanocytic antigens have been detected in the sera of vitiligo patients[7,8]. These antibodies have been shown to cause destruction of melanocytes in vitro by means of complement-mediated lysis and by antibody dependent cellular cytotoxicity[3]. In addition to this destructive effect autoantibodies targeting the melanocyte function have also been reported in patients with vitiligo. These include the antibodies against tyrosinase, tyrosine related peptide 1 and 2, Pmel 17 and melanin concentrating hormone1 [MCHR1][3].

As far as the cell mediated immunity is concerned the evidence of a pathogenic role is even more convincing. In fact, if there is anything that has really come close to be called the melanocyte killer in vitiligo, it is the 'T-lymphocyte'. Activated cytotoxic T-lymphocytes have been consistently reported in abundance in the lesional as well as perilesional skin in vitiligo patients[9]. These lymphocytes are predominantly CD8+ cytotoxic T-cells and express skin homing receptors (CLA+). Moreover, these lymphocytes are seen in close apposition to the disappearing melanocytes[9]. Additionally, cytotoxic T-cells have been demonstrated against melanosomal proteins like Melan A, Mart 1, gp 100 and tyrosinase in vitiligo patients[10].

Evidence of T-cell activation in vitiligo has also come indirectly through demonstration of elevated levels of IL-6, IL-8 and serum soluble IL-2 receptor in the sera of vitiligo patients[11,12]. In the lesional skin also the levels of IL-2, IL-6 and TNF-á are increased consistently in these patients[13]. What is more, when the vitiliginous skin is treated with twice daily application of tacrolimus, a topical immunomodulator, the levels of lesional TNFá expression are significantly decreased and this correlates well with the evidence of repigmentation in the affected area[14].

Genetic studies

Genetic studies have all along supported a non-mendelian inheritance

are seen on the exposed parts of the body like the face and neck and the acral parts of the body respond the least. Pimecrolimus has also been tried in vitiligo in the recent past and the results with this congener have been almost the same[11].

Pseudocatalase

Pseudocatalase has been used in combination with Dead Sea climatotherapy or UVB exposure for the treatment of vitiligo. The basis for the use of this agent in vitiligo is an evidence of oxidative stress and high H_2O_2 levels in the lesional skin. While some earlier studies[12, 13] demonstrated excellent results with this agent in inducing repigmentation in vitiligo later studies have cast doubts on its efficacy[14]. Pseudocatalase is used topically on the lesional skin and this is followed by UVB exposure to the whole body or to the lesional skin. The combination is claimed to correct the oxidative stress on melanocytes in vitiligo patients and thus lead to correction of the depigmentation.

SURGICAL THERAPIES

Surgical therapies for vitiligo have further increased the percentage cure of the disease by an appreciable degree. With the result their use is on the increase in the management of unresponsive vitiligo both in India and abroad. These surgical therapies, as a rule are indicated in those patients who have a stable [non-progressive] disease of at least one year, not responding to medical treatment. The most important advantage with these procedures in general is that the chances of repigmentation of lesions are in the range of 90-100%. What is more, these interventions are becoming better and easier to perform with every passing day.

Different surgical therapies that have been tried in the management of vitiligo include autologous suction blister grafting, split-thickness grafting, punch grafting, smash grafting, single follicular unit grafting, cultured epidermal suspensions and autologous melanocyte culture grafting. All these grafting procedures, except the melanocyte culture grafting, are easy to perform and do not require any sophisticated instruments.

Suction blister grafting

Here, thin epidermal grafts are taken from suction blisters on the donor site, usually on the buttocks or thighs. These suction blisters are produced by applying a sufficient negative pressure on the skin at the donor site by using a suction apparatus or syringes with 3-way cannulae. The epidermal grafts are then transplanted on to dermabraded vitiligo lesions. This leads to repigmentation of the recipient areas with an excellent cosmetic matching. The ease of the procedure, the high success rate and the excellent cosmetic results have all made suction blister grafting the procedure of first choice in vitiligo grafting[15].

Split thickness grafting

In this grafting technique a thin split thickness graft is taken from a donor site with the help of a dermatome, Humby's knife or a simple shaving blade. This graft is then transplanted on to dermabraded recipient areas. This technique also gives an excellent cosmetic matching after repigmentation and the incidence of repigmentation in this technique is also quite high. In fact, most comparison studies on grafting techniques in vitiligo have shown that maximum repigmentation is achieved with either suction blister grafting or split thickness grafting[15].

Punch grafting

Here full-thickness punch grafts of 1.0 to 2.5cm diameter are taken from a suitable donor site and then transplanted on to similar punch shaped beds on the recipient vitiligo lesions. The recipient area is then treated with either PUVA/PUVASOL or topical steroids leading to spread of pigment from the transplanted punches to the surrounding skin. With time the whole of the recipient area gets repigmented. The advantages of this procedure are that it is easy to perform and can take care of a relatively larger vitiligo area as compared with the above two procedures. However there are certain limitations as well as there are chances of 'cobblestone appearance', 'polka-dot appearance' and hypertrophic changes at the recipient site[16]. All these side effects can be minimized by proper patient selection and by use of smaller sized punches of 1.0 to 1.5 cm diameter.

Follicular unit grafting

In this technique, single-hair follicular units are harvested/prepared from a suitable donor area as in case of hair transplantation. These follicular units are then cut above the level of the follicular bulb and then transplanted into vitiligo lesions. The idea behind this technique is that the melanocytes in the follicular unit get 'donated' to the vitiliginous skin and serve as a source of pigment at the recipient site. The repigmentation process here simulates the normal process of repigmentation of vitiliginous skin quite closely and thus gives an excellent cosmetic result. The procedure thus combines the advantages of punch grafting with the excellent cosmetic results of split thickness or blister grafting techniques. The procedure is however tedious and needs a good expertise on the part of the cosmetic surgeon.

Cultured Epidermal Suspensions

Here a split-thickness graft is taken from a donor area and then incubated overnight. On the next day the cells are mechanically separated using trypsin-EDTA solution and then centrifuged to prepare a suspension. This cell suspension is then applied to the dermabraded depigmented skin area, and a collagen dressing is applied to keep it in place. A relatively large area of vitiligo, about ten times the size of the donor graft can be taken care of with this procedure[17]. The recipient area however has to be treated with either NB-UVB or PUVA for two to three months to achieve the desired pigmentation.

Melanocyte Culture Transplantation

This is a relatively more advanced grafting procedure where, once again, a split-thickness graft is taken from a donor area and incubated in appropriate culture medium to grow the melanocytes or the keratinocytes-melanocyte combination in vitro. The cultured cells are then applied on to laser dermabraded or even mechanically abraded lesional skin[18, 19]. The procedure is obviously more difficult to perform, as it needs the advanced lab facilities for melanocyte culture. However the results with this procedure are excellent and a relatively large area of involved sin can be taken care of by a single donor graft.

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Trends of tinea capitis in population attending dermatology department of a tertiary health care facility in Kashmir

Mubashir Maqbool Wani, Qurat-ul-Ain Kamili, Muhsin Chisti, Mudasir Maqbool Wani & Qazi Masood

ABSTRACT

The present epidemiological study spanning a period of 10 months (aug"04 to may"05) is based on 18,043 patients who attended dermatology OPD at SMHS during the said period. Among 18,043 patients seen, 2,136 patients were suffering from fungal infections in general and among them 781 had Tinea capitis. The study also reveals higher incidence of infection in cooler months. The disease peaks in January. The disease is highly prevalent in the age group of <10years (72%), seen more in rural (73%) than in urban (27%) and more in males (61%). These findings may have an important implication as a measure of disease control and as a guide for prevention policies especially in winter.

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INTRODUCTION

Tinea capitis or "ring worm" of the scalp is a disease in which the essential feature is invasion of hair by a dermatophyte fungus. Causative organisms include *T.Tonsurans, M.Audoinii, T.Schoenleni and T.Violaceum.* Tinea capitis is world wide in distribution. It is quite contagious and is generally spread by person to person contact. The organism has also been isolated from such inanimate objects such as hair brushes and pillows. There may be racial differences of susceptibility but they are not clearly established [1]. From the classical experimental work of Kligman[2,3] on *M.audouinii*, it is clear that if actual hair infection is to occur, invasion of stratum corneum of the scalp skin must first develop. Trauma assists inoculation, which is followed, after approximately 3 weeks, by clinical evidence of hair shaft infection. Spread to other follicles proceeds, then for a period of variable duration the infection persists, but does not spread further. The incidence of Tinea capitis has been increasing and presents a growing public health concern. The findings of this study could influence programmes of health education and health promotion.

METHODS AND PATIENTS

Data based on 18,043 patients attending dermatology OPD from August"04 to May"05 was analised to find the relationship of Tinea capitis vis-à-vis different parameters as seasonality, age, sex and rural urban distribution and to deduce a relevant correlation if any *[see table 1]*

Diagnosis of Tinea capitis was based on the clinical presentation, microscopic visualization of the fungus by KOH preparation and culture on Sabouraud's agar.

Table I

Month	Total no. of New cases seen	Patients with Fungal-infection	Patients with Tinea capitis	Sex		Age		Location	
				Male	Female	<10	>10	Rural	urban
August"04	2217	292	40	24	16	29	11	31	9
September"04	2385	254	65	39	26	46	19	51	14
October"04	1560	159	52	29	23	37	15	39	13
November"04	2066	244	97	48	49	76	21	73	24
December"04	1629	220	98	56	42	71	27	80	18
January"05	1025	130	71	52	19	54	17	48	23
February"05	1674	198	93	62	31	68	25	55	38
March"05	2182	272	124	77	47	85	39	94	30
April"05	2361	237	98	65	33	67	31	76	22
May"05	944	130	43	24	19	31	12	27	16
Total	***18,043***	***2,136***	***781***	***476***	***305***	***564***	***217***	***574***	***207***

OBSERVATIONS Of the total fungal infections reported (2136 patients), 781 had Tinea capitis (36.56%) *see figure 1.*

The seasonal incidences are presented in *figure 2.* Rates (Tinea capitis cases per 1000 patients) have been plotted against average temperature (provided by meteorological department Srinagar) in respective months. The monthly rates varied from a low of 18 cases of Tinea capitis per 1000 patients in august to a high of 69.26 Tinea capitis cases per 1000 patients in January.

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Keywords: Tinea capitis, epidemiology, seasonality, age, sex, rural urban distribution.

Study revealed that most of the cases of Tinea capitis were in the age group < 10 years (72%). *see figure 3*

The infection was present more commonly in males (61%) as compared to in females (39%). *see figure 4* .

SAMPLE	X	N	SAMPLE P
1	359	6394	.056146
2	249	7907	.031112

Estimate for p[1]–p[2]: .025034
95% CI for p[1]–p[2] : .0182169,.0318526
test for p[1]–p[2] = 0 vs not = 0
Z = 7.20 p – value < .0001 C I Confidence interval

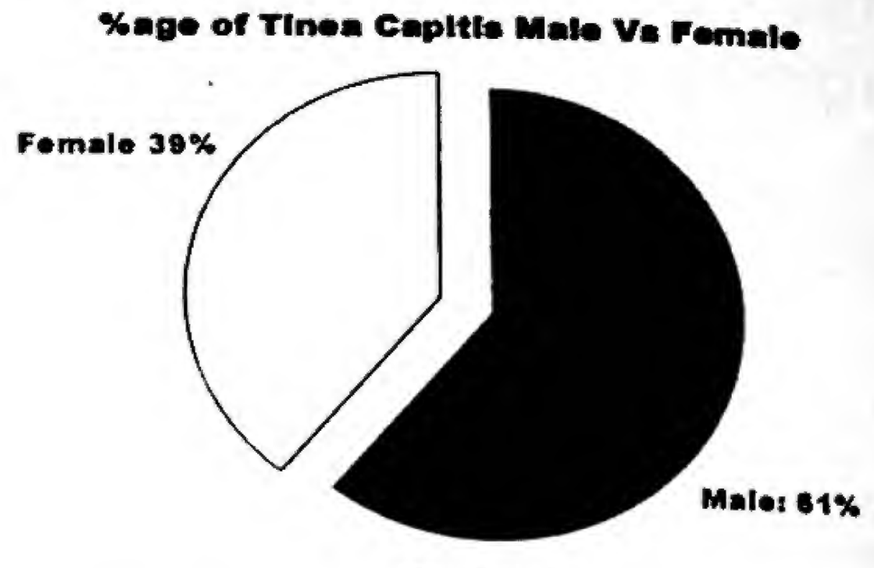

Figure 4

73% of patients presenting with Tinea capitis had a rural background. *See figure 5* .

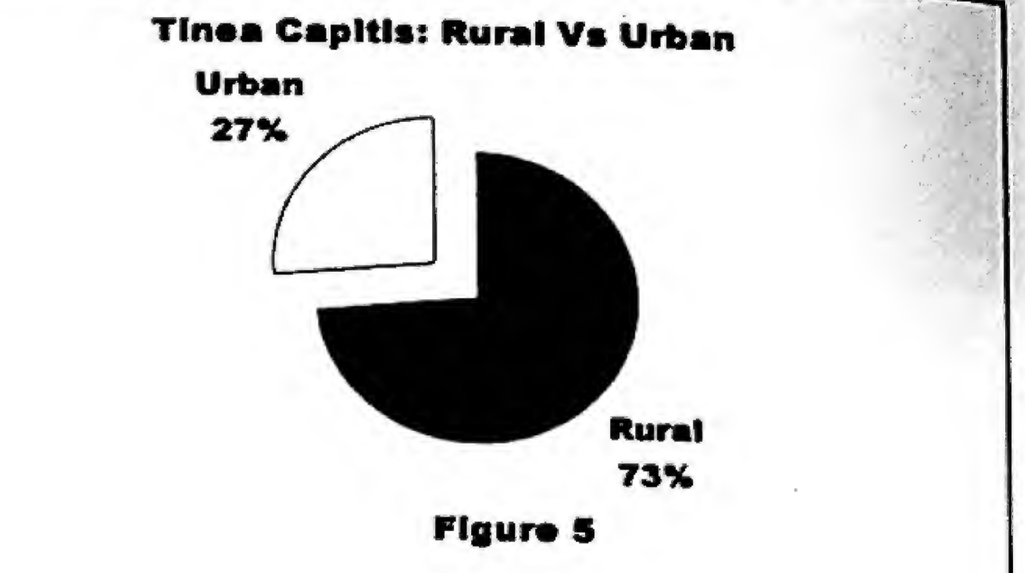

Figure 5

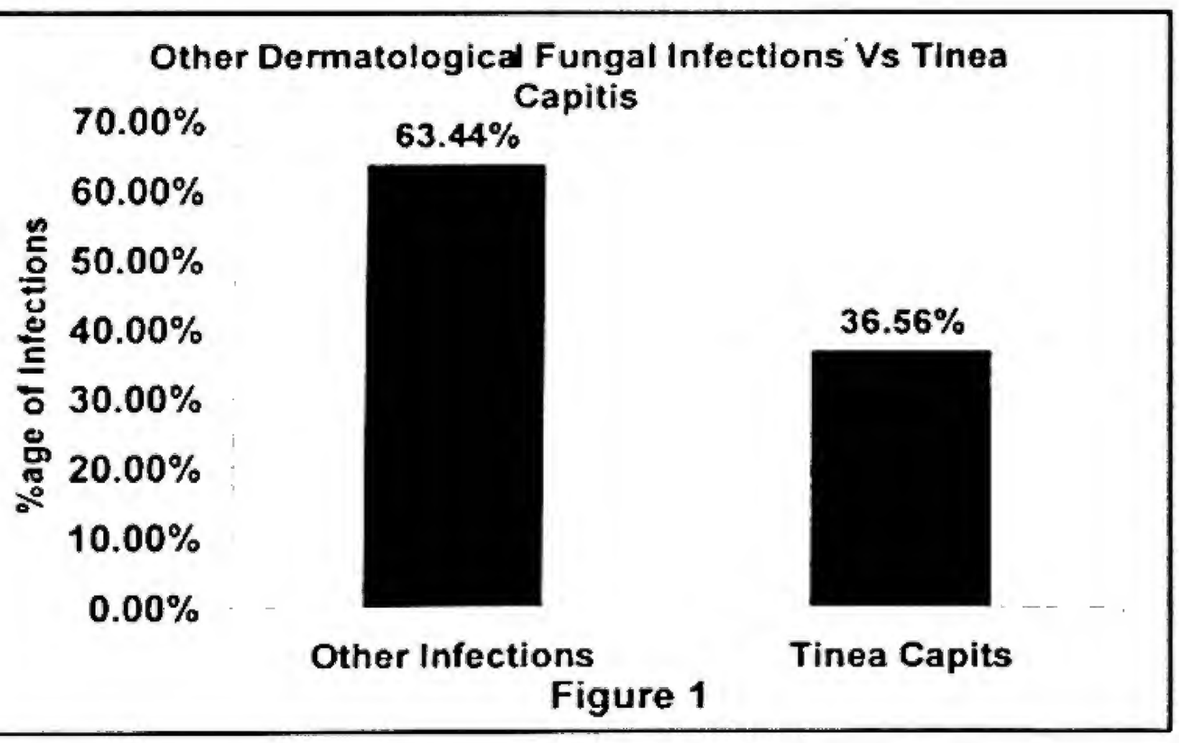

Figure 1

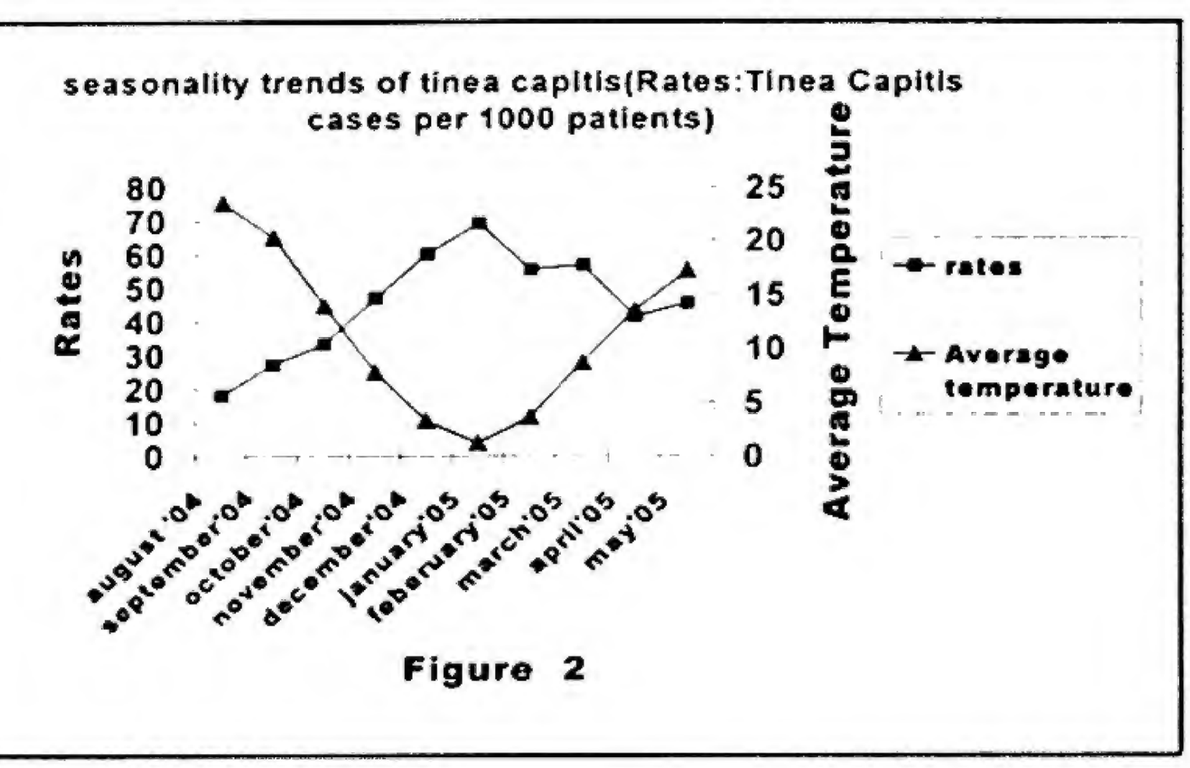

Figure 2

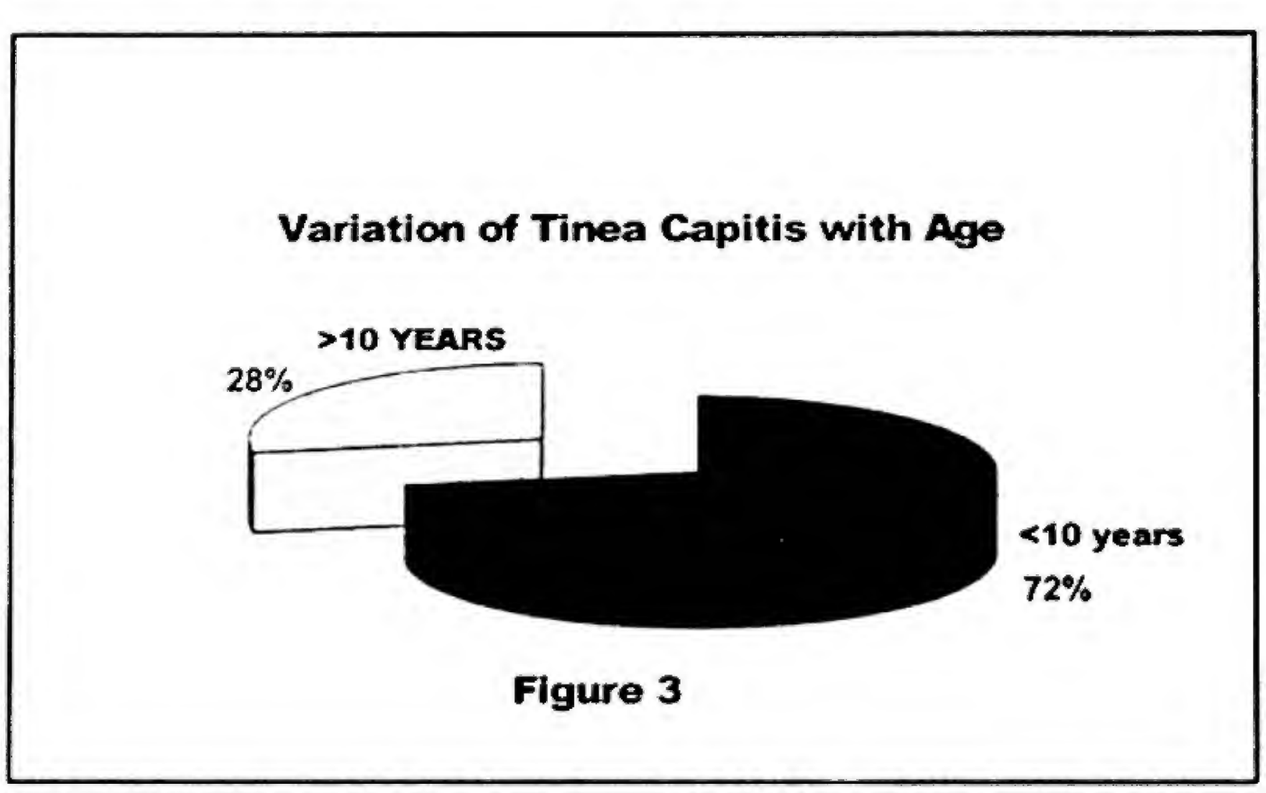

Figure 3

STATISTICALANALYSIS

A two tailed test for difference between two proportions was carried out under the null hypothesis that the proportions are equal p1 = p2 against an alternate hypothesis p1 not = p2 where p1 is the proportion of diseased person in winter (Nov"04 to Feb"05) and p2 is proportion of diseased in summer (April '05, May"05 Aug"04, Sep"04) using test statistic Z. On the basis of Z value (7.20) and P value (<.0001) the null hypothesis is out rightly rejected. Thus the disease is more in winter than in summer. This was done using mini tab software.

DISCUSSION

Although these epidemiological trends may be attributable to living conditions in winter, biological factors of the fungus may have a role.

Living conditions of a typical rural family in winter are synonymous with poor hygiene, poverty, overcrowding, increase in interpersonal contact which means increase in the spread of the disease.

One strong explanation for such a high prevalence of the disease in children in this part of the world is because of the habit of shaving off heads of children during winter. Though conclusive proof gained by prospective studies is not yet available but this is supported by clinical experience. Shaving is done with a common blade (*KHOOR*) especially in rural areas. Using a common blade helps in spread as well as inoculation of the fungus which is followed after approximately 3 weeks by clinical evidence of hair shaft infection [2,3]. So in winter they in particular get the disease and then it spreads very rapidly. Thus a typical sufferer of Tinea capitis in our set up is a child <10 years, rural male presenting in winter with a history of head shaving or exposure to one of his siblings who has same history.

Over all fungal infections are less common in females which may be partly due to less exposure to an environment conducive to spread of infection.[4,5,6].

CONCLUSION AND RECOMMENDATIONS

The results of this study emphasize and impress upon the status of Tinea capitis as a public health problem. The magnitude of the problem calls for a proper health policy aimed at prevention and control rather than cure.

Cure of Tinea capitis in our setup means giving Griseofulvin which has disadvantages like poor compliance because of cost, length of treatment, its bitter taste in liquid form, photosensitivity and gastro intestinal side effects.

Giving up the habit of sharing of blades, shunning the use of KHOOR, improving hygiene and raising standard of living among population are key to prevention.

GLOSSARY

KHOOR – Kashmiri term used for common blade. It is used mostly by barbers in rural areas, its edge is sharpened on a rubber pad or on a flat stone (*BELAU*). It is used again and again for shaving and does not carry any provision for putting on a new blade. Besides it being a mode of spread for Tinea capitis, it also carries a potential for spreading diseases like HIV, Hepatitis B & Hepatitis C. Its use is highly condemnable and should be discouraged.

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Clinical study and management of haemopneumothorax in Kashmir

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ABSTRACT

100 cases of haemopneumothorax, were studied Haemopneumothorax mostly due to trauma with few cases of spontaneous haemopneumothorax. Patients of all age groups with peak age of 20-40 years (52%) with a sex ratio of 1.85:1. 70 percent followed blunt trauma, 25 percent penetrating chest trauma and only 5% of cases were spontaneous. Chest pain was the most frequent symptom (80%) followed by dyspnoea (56%) shock was less frequent in blunt trauma (14%) than in penetrating trauma (32%). 11 percent patients presented with acute abdomen which was again significantly more common with penetrating trauma.Chest radiograph and needle thoracentesis was the main modality of diagnosis. 70 percent patients were managed conservatively with intercostal chest drainage(ICD), needle thoracentesis, I.C.D. with intrapleural fibrinolysis therapy, external stabilization of chest and observation only. 30 percent patients underwent surgery among these 23 percent were associated with abdominal injury which merited exploratory laparotomy Early thoracotomy was performed in only one patient of blunt trauma chest . 4 percent in whom combined theracoabdominal exploration was done through separate incision in view of associated internal visceral injury. 5 patients (20 percent) of penetrating chest trauma were managed with early thoracotomy in view of persistent haenmorrhage through the chest tube drain in 4 patients and one patient had diaphragmatic tear on right side with associated liver injury. Intercostal chest tube drainage with intrapleural fibrinolytic therapy was given in 9 patients with an overall success rate of 87.5%. 2 percent patients underwent late thoracotomy with decortication after 8 weeks . One patient had unsuccessful fibrinolytic therapy for clotted haemothorax and another patient developed empyema following blunt trauma chest treated with intercostal chest tube drainage initially Most frequent complications seen were residual fluid collection or thickened pleura 6% wound infection and pneumonia 6% and 3% respectivelyMortality in our series was 9% which was primarily related to haemorrhage, shock and multiple injuries in these patients.

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Introduction :-

Haemopneumothorax involves accumulation of air and blood within the pleural space. It can occur following trauma or in the absence of trauma or other obvious causes when it is called spontaneous haemopneumothorax. Traumati haemopneumothorax can be due to blunt trauma or penetrating injury . Blunt trauma falls (at home, from windows, on stairs, on the street) is the common cause. Automobile injuries to passenger or pedestrian , assaults, injuries by kicking and by blunt instruments are other major mechanisms.

In penetrating chest trauma, gunshot wounds and stab wounds constitute the majority of injuries[1]. Spontaneous haemopneumothorax is a rare disorder occurring in 1 % to 12% of patients with spontaneous pneumothorax[2] A spontaneous pneumothorax can be primary without known etiology or clinical evidence of an underlying disease or secondary to a disease process that predisposes to pneumothorax[3]

The two mechanisms of bleeding in spontaneous haemopneumothorax are :-

1. Bleeding as a results of a torn adhesion between the parietal and visceral pleura[4]
2. Rupture of vascularized bullae

The goals of treatment in haemopneumothorax include haemostasis and reexpansion of the lung . Initial treatment consists of resuscitation with adequate fluid replacement and drainage of the pleural space which involves needle drainage, closed intercostal chest tube drainage, closed intercostal chest tube drainage with intapleural fibrinolytic treatment and some patients with minimal collection need only observation.

A thoracotomy provides opportunity to

1. Stop the bleeding and evacuate coagulated blood from the pleural cavity.
2. Seal the site of air leak on the lung surface.
3. Secure effective drainage by drain placement under direct vision. With this background knowledge of haemopneumothorax an endeavor has been made to evaluate and study in detail this clinical condition in our hospital.

Material and Methods :-

The study was undertaken is CVTS division of the department of Surgery SMHS

Keywords: Haemopneumothorax, intercostal chest drainage, thoracotomy.

Fig 1. Forearm injury chest with sucking wounds

Hospital Srinagar during the period ranging from 2001 to 2003 AD. 100 patients received in the emergency department were studied. A thorough history about mode of trauma and other relevant history and detailed clinical examination was done. In haemodynamically unstable patients, resuscitation was started at the outset consisting of mainly maintaining breathing, circulation, replacing blood loss, controlling sucking wounds and drainage the pleural space with simultaneous and continuing appraisal of possible visceral injury in the chest as well as abedomen. Wise and prompt surgery was done wherever necessary . The patients were examined for any complications during follow up for 3 to 4 months.

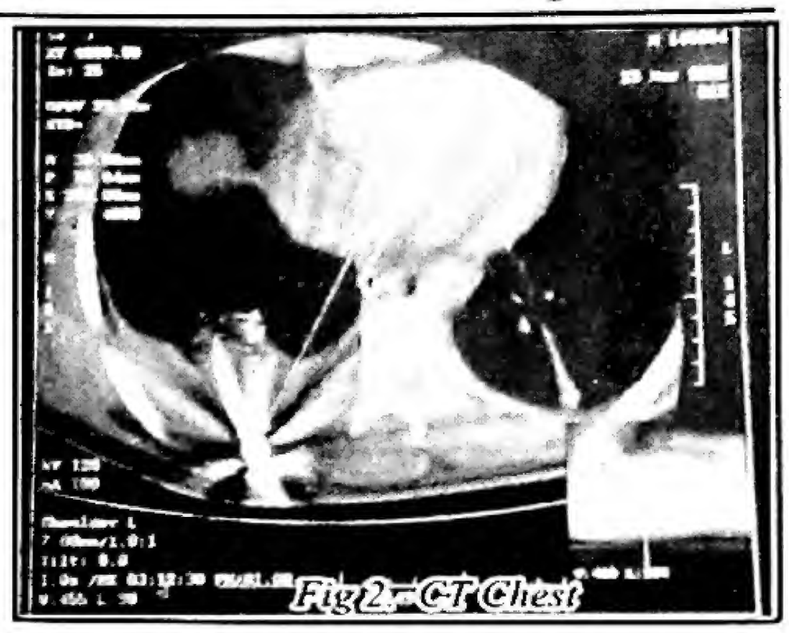

Fig 2. CT Chest

Fig 3.

Clotted Haemothorax with trapped lung.

Fig 4.

Intra operative view of decortication

Table I : TREATMENT OF HAEMOTHORAX (n = 100 cases)

Treatment	Blunt Trauma N=70	Penetrating trauma		Spontaneou N = 5	%age
		Missile wounds N=23	Stab N=2		
Resuscitation and treatment shock	10	0 8	-	01	19%
Closed Intercostal tube drainage only (CID)	39	08	01	04	52%
CID followed by thoracotomy	-	04	-	01	5%
CID and abdominal exploration	11	08	01	-	21%
Combined Theracoabdominal exploration	01	01	-	-	2%
Needle drainage (Alone)	04	-	-	-	4%
CID with intrapleura fibrinolytic treatment	08	01	- 1	-	9%
Decortication	01	01			2%
Observation only	02			2%	
CID with external Stabilization of chest	04				2%

In intrapleural fibrinolytic therapy, streptokinase 250000 IU was diluted in 100ml of normal saline solution and administered through the chest tube. The chest tube was clamped for 4 hours and the patients were mobilized during the period to allow a better distribution. After 4 hours period, the clamp was removed. This procedure was repeated everyday until radiographic improvement was achieved.

Results and Discussion :-

Maximum patients in our study belonged to age group of 3rd and 4th decade (20% and 32%) with a sex ratio of 1.85 : 1.70 percent had blunt trauma, 23 percent penetrating trauma due to firearm injury, 2 percent stab wounds and 5 percent were without any history of trauma or any other obvious cause. Out of blunt trauma group 35 (50) percent patients had automobile injuries and 2 (2.8%) patients had history of alleged assault . Out of penetrating chest injuries majority had injury due to gunshot wounds, bomb splinters and booby trap mines (IED). In firearm injuries,

Table 2

Complication	Non Penetrating (blunt) trauma n = 70	penetratin trauma n = 25		Spontaneous n=5	Percent
		Missile Wounds (n =2)	Stab wound (n-23)		
Pneumonia	02	01	-	-	3%
Residual fluid or thickened pleura	05	01	-	-	6%
Empyema	01	-	-	-	-
Clotted Haemothora	02	01	-	-	3%
Wound infections	02	03	01	-	6%
Pulmonary edema (ARDS)	01	-	-	-	1%

wound of entrance was in abdomen in majority of patients in our series with one instance of wound of entrance in neck and shoulder. In two cases of penetrating stab wounds, one injury was inflicted by knife and other by a sharp iron rod.

Wounds were multiple in 10 cases (40%) although not all multiple wounds were penetrating and occurred at every conceivable location on chest, front, back, axilla etc. Neck wounds were typically low in supclavicular fossa and shoulder and abdominal wounds were directed towards chest. Clinically patients presented with chest pain (80%), shortness of breath 56%, shock (19%), acute abdomen 11%. Physical signs included diminished to absent breath sounds 45%, fracture ribs (78%) , subcutaneous emphysema (34%), hyper resonant percussion note (11%), Dullness to percussion (32%), local wound haematoma (12%), significant soft tissue injury to chest wall (61%), obvious chest wall instability (4%), sucking wounds (4%), cyanosis (9%), pallor (23%), haemoptysis (4%), lethargy, stupor or coma in 13% patients primanly due to shock and associated injuries especially head injury.

At the time of admission, these patients were given resuscitative measures as per the clinical status of the patient. The treatment included maintenance of airway, breathing, blood and fluid replacement for shock and then pleural drainage. In 19 percent patients chest wall stabilization was accomplished by external methods in conjunction with intercostal blocks in 3 patients of blunt trauma and assisted positive pressure ventilation in one patient. Further surgical management was done as is shown in the table I

In our series maximum 6 doses of streptokinase were administered for intrapleural fibrinolytic therapy and chest tube was removed when the pleural drainage was 50ml in 24 hours. There was no complication in IPFT. Coagulogram and platelet count was done in each patient before subjecting to IPFT. Only one patient underwent decortication in view of unsuccessful fibrinolytic therapy

The complication that occurred during the management of haemothorax are depicted in Table 2

The mortality was 9 percent in our series and the cause of death is depicted in table3

Early mortality was due to haemorrhage, shock and multiple injuries whileas later the pulmonary complications and sepsis was more important cause of death in haemopneumothorax patients.

The incidence of chest trauma is high in our valley because of increase in automobile accidents and violence. However, we reported 5 cases of haemopneumothorax who were spontaneous. Haemopneumothorax can develop in 1 to 12 % of patients of spontaneous pneumothorax[3]

Chest pain and shortness of breath (80%) was the main complaint in our series more so in blunt trauma John et al[1] reported chest pain and shortness of breath each in approximately 50% of all patients.

Table 3

Cause of Death	Non penetrating Blunt (trauma) n=70	Penetrating trauma n=25		Spontaneous n=5	Percent
		Gunshot wounds (n=23)	Stab wounds (n=2)		
Haemorrhage and associated poly trauma	03	02			5%
Pulmonary Complication (pneumonitis, ARDS)	01	02			3%
Head injury	01				1%

Shock was recorded less frequently in chest blunt trauma (14 percent) than in patients with penetrating injuries (32 percent)

Summary and Conclusion :-

Majority of patients with haemopneumothorax had chest trauma but it can also develop spontaneously as in 5 percent patients in our series.

Patients belonged to all age groups with peak age of presentation 20-40 years (52%)

70 percent cases followed blunt trauma and 25 percent has penetrating chest trauma.

70 percent of patients were managed with intercostal chest tube drainage, needle thoracentesis, intercostal chest drainage with intrapleural fibrinolytic therapy, external stabilization of chest and observation only. 30 percent patients needed further surgical intervention . Among these, 23 percent had associated abdominal injury which merited exploratory laparotomy.

Associated intraabdominal injuries were more frequent with penetrating chest trauma 44 percent than blunt trauma17%

The abdominal organ commonly injured was liver followed by diaphragm and spleen.

In patients with blunt trauma early thoracotomy was

performed in only one patient 1.4 percent in whom combined thoraco abdominal exploration was done through separate incisions in view of associated abdominal injuries.

5 patients (20%) of penetrating chest trauma were managed with early thoracotomy in view of persistent haemorrhage through chest tube drain in 4 patients and one patient had diaphragmatic tear on right side with associated liver injury.

Intercostal chest tube drainage with intrapleural fibrinolytic therapy was given in 9 patients with an overall success rate of 87.5 percent.

2 percent patients underwent late thoracotomy with decortication after 8 weeks. One patient had unsuccessful fibrinolytic therapy for clotted haemothorax and another patient developed empyema following blunt trauma chest treated with intercostal chest tube drainage initially.

Most frequent complication seen were residual fluid collection, or thickened pleura (61%) wound infection (61%) and pneumonia (3%).

Mortality in our series was 9 percent which was primarily related to haemorrhage, shock and multiple injuries in these patients.

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Transrectal Ultrasonography of Prostate -Correlation with Histopathology

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ABSTRACT

One hundred patients with clinical signs/symptoms of prostatic disease were subjected to TRUS and correlated with histopathological findings. TRUS revealed BPH in 65, chronic prostate in 5, suspicious carcinoma in 23, rest normal. HPE confirmed BPH in 62, chronic prostatitis in 2 and carcinoma in 11. TRUS sensitivity and specificity for prostatic carcinoma was 81% and 54% respectively. TRUS + PSA assay were most accurate in detecting and staging prostatic carcinoma.

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INTRODUCTION

Transrectal ultrasonography is twice more sensitive than digital rectal examination for detecting prostatic carcinoma. TRUS provides for direct visualisation of echopattern site and size of lesion and also helps in proper interpretation of PSA levels which may be raised in many benign conditions especially BPH. TRUS along with PSA could become a sensitive and specific tool for screening prostatic carcinoma.

MATERIAL AND METHODS

One hundred patients referred from Urology department were examined by transrectal USG using Siemens Adara 7-12 MHz phased array probe over last two years. Patients were examined with full bladder with properly lubricated transrectal probe wrapped with a condom in left lateral daeubitus position. The prostate and adjacent rectal bladder walls were evaluated for any focal lesion, change in echogenecity. Lesions seen on USG were correlated with HPE, PSA assay and DRE.

RESULTS

Table 1: Sonographic features in TRUS

BPH	Hypocchoic	9
	Hyperechoic	6
	Isoechoic	50
Ca Prostate	Hypoechoic	14
	Hyperechoic	7
	Isoechoic	1
	Mixed	1
Chronic prostatitis	Mixed with calcification	7
	Normal	7

Table 2: TRUS findings with HPE correlation (Fig. 1, 2, 3)

TRUS diagnosis	HPE Normal	BPH	Ca prostate	Chr. Pros.	%
BPH (65)	-	62	3	-	94
Chronic prostitis (5)	3	-	-	2	40
Suspicious carcinoma (23)	4	-	13	6	56
Normal prostate(7)	-	-	-	-	100

Table 3: Correlation of DRE abnormality, PSA & TRUS findings

DRE	Serum PSA	TRUS findings
Induration	1-4 nmol/ml	Increased echogenicity (5) with prostitis
Nodular prostate	4-10 nmol/ml	Ca prostate 5 Normal 3
Mucosal fixity	> 1nmol/ml	Ca prostate 2 Lesion > 1.3 cm

Table 4: Correlation with PSA levels

DRE + increased PSA levels	Suspicious carcinoma	= 20
DRE + increased PSA + TRUS findings	Suspicious carcinoma	= 16
Histopathological proved		= 11 cases

DISCUSSION

With the description of zonal anatomy by McNeal [1] and advent of transrectal sonography, the various pathological processes became better defined especially for

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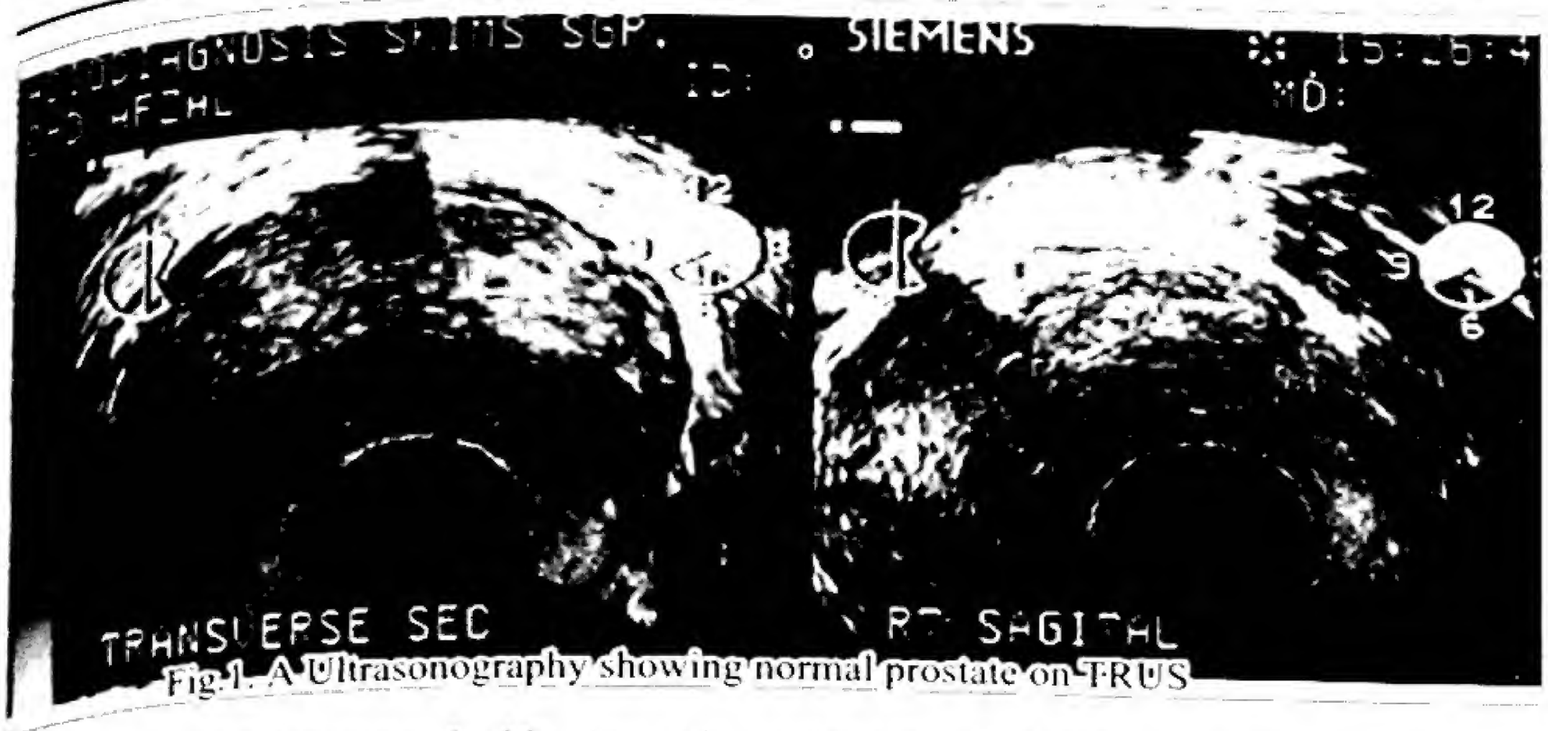

Fig.1. A Ultrasonography showing normal prostate on TRUS

screening for nonpalpable prostatic carcinoma. Earliest studies in TRUS showed prostatic carcinoma predominantly is an echogenic lesion [3]. Benign lesions like BPH were limited to transition zone and appeared mostly as a diffuse textural changes [4].

In our series prostate carcinoma appeared mostly as echogenic focal lesion in the peripheral zone in 23 patients out of which 13 proved correct on histopathology. Three cases were false negatively labelled as BPH and proved to be carcinoma.. None of the normal cases on TRUS had evidence of carcinoma in HPE.. There was a positive correlation between TRUS findings suggestive of carcinoma, Digital rectal examination and PSA

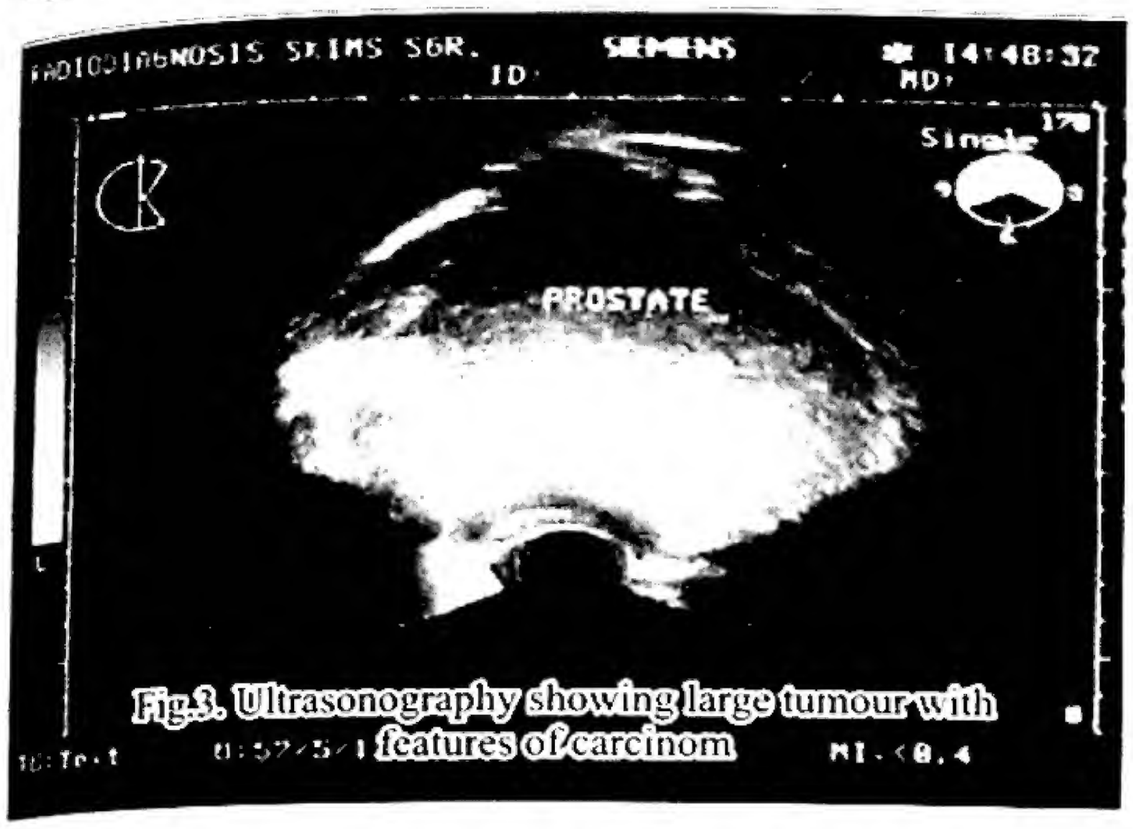

Fig.3. Ultrasonography showing large tumour with features of carcinom

levels. Thus 7 out of all the focal lesions in TRUS had positive DRE and raised PSA levels of more than 5 nmol/ml.

JS Wolf [6] demonstrated increased accuracy of combined staging method using TRUS and PSA. The size of the focal lesion was related to serum PSA levels e.g., two focal lesions > 2.0 cm had PSA levels in excess of 1nmol/ml. Cooner et al [5] found 45 cases out of 144 screened by TRUS with PSA levels > 10 ng/ml having prostatic carcinoma and concluded that every patient with significantly raised PSA levels should have TRUS examination. All the four focal lesions > 1.5 cm3 volume had raised PSA levels of >10 nmol/ml, two having invasion of prostatic capsule suggesting that size of the lesion was related to glisson state of the lesion.. Petter Littrays et al [7] suggested close

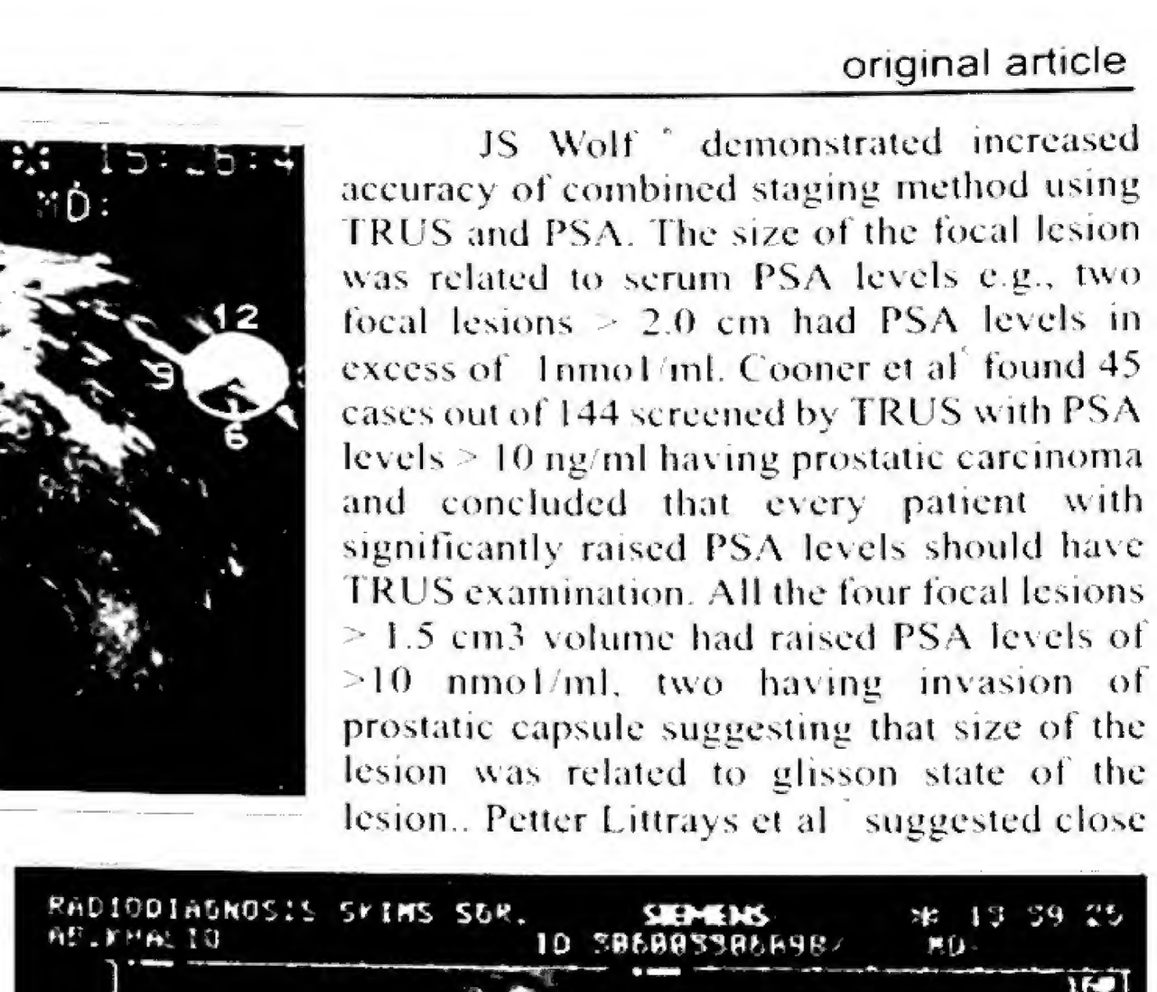

Fig.2. Ultrasonography showing median lobe projecting into the bladder

relationship of prostatic volume to PSA levels. Wolf et al [6] showed that the volume of hypoechoic lesion as an independent variable for staging of carcinoma prostate.

Use of combination modality screening such as DRE + PSA and TRUS + PSA showed increased accuracy compared to DRE or TRUS as stand alone modality. Twenty of patients in our series were positive for carcinoma prostate using DRE + PSA while 16 out of these were positive in TRUS + PSA screening. Histopathology proved eleven of these patients to have prostatic carcinoma. Thus TRUS + PSA significantly scores over as a screening combination. Wolf et al [6] showed that by combining prospective TRUS evaluation with retrospective PSA analysis, there was increased accuracy of this combined staging / screening method compared to TRUS alone.

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Amino-Acid Infusion in Oligohydramnious

Abida Ahmad

ABSTRACT

Oligohydramnios is a rare condition where the liquor amnii may be reduced to a few ml. of viscid fluid. This is a late sign of foetal malnutrition. Oligohydramnios or diminished liquor is quite often associated with impaired foetal growth, foetal anomaly and malpresentation.

The study was done to see whether maternal nutrition plays any role in maintaining the foetal environment, 20 patients of oligohydramnios in third trimester were selected for the present study. Maternal nutrition was improved by parenteral amino acid infusion. A significant improvement was observed subsequently as the AF1 was seen to increase and less operative intervention was needed. A lesser perinatal mortality was as well seen.

JK-Practitioner 2006;13(3); 140-141

Introduction

Amniotic fluid surrounds the foetus in uterus and forms a protective cushion around it. The volume normally increases to about a litre around 36 weeks but decreases thereafter till term. In oligohydramnios the volume of amniotic fluid may fall far below the normal limits and occasionally be reduced to only a few ml. of viscid fluid.

Oligohydramnios is said to be a late sign of fetal malnutrition. Foetal well being to a great extent depends upon the appropriate volume of amniotic fluid. Oligohydramnios in early pregnancy is attended by serious consequences to the foetus. Subjected to pressure from all sides the foetus assumes a peculiar appearance and musculoskeletal deformities such as club foot, talipes and wry neck may be seen. The skin of foetus appears dry, leathery and wrinkled. Pulmonary hypoplasia is common with oligohydramnios [1] Diminished liquor is quite often associated with impaired foetal growth, foetal anomaly and malpresentations. This is also associated with abnormal FHR pattern and muconium staining of liquor which often requires caesarean section and results in perinatal mortality and morbidity.

Different medical and interventional methods have been tried to treat oligohydramnios. The present study was done to see the effect of amino acid infusion on amniotic fluid index, mode of delivery and foetal outcome.

Material and Method

The study was done on 20 clinically and sonographically proven cases of oligohydramnios in third trimester of pregnancy, in the department of Gynaecology and Obstetritcs at Sher-i-Kashmir Institute of Medical Sciences, Soura, Srinagar.

Patients with gestational age of more than 28 weeks and less than 36 weeks were taken for the study. Patients with any congenital anomaly of foetus, maternal pulmonary, cardiovascular and abdominal pathology or premature rupture of membranes were excluded from the study.

Amniotic fluid volume was measured with four quadrant technique which consists of measuring the largest pool of fluid found in each of the four quadrants of uterus. The added measurements give AFI. The fluid is decreased when AFI is less than 10cms and markedly decreased if less than 5cms. [2].

A detailed obstetric, menstrual, past, personal and family history was taken. General systemic and obstetric examinations were conducted. Abdominal girth and fundal height was measured in cms. and recorded weekly. A record of foetal movements and foetal heart was maintained.

All investigations of blood i.e. Hb, ABO, Rh, TLC, DLC, BT, CT, VDRL, KFT and Sugar were done. Routine urine examination with culture/sensitivity as and when needed was also done. After initial USG, patients in the study group were subjected to repeat USG weekly. The patients in study group were given I/V infusion of 200 ccs of aminoacid on alternate days for the first week and repeat infusions were given after 2-3 weeks if required. Each patient received 500ml of 10% Fructodex prior to amino acid infusion. Oral iron, calcium and multi-vitamin therapy was continued as before. The patient were followed till delivery.

Observations

Patient at entry were divided into two groups:

a) Moderate oligohydramnios (AFI: 5.1-10 cms)
b) Severe oligohydramnios (AFI < 5cms).- *(Table-I)*

All the patients with severe oligohydramnios had IUGR, whereas 60% of patients with moderate oligohydramnios had IUGR (Table-II). 5(33.00%) patients

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Keywords: Oligohydramnios, less liquor amnii, amniotic fluid, foetal well being, amniotic fluid index (AFI).

Table-I: Grouping of patients according to AFI

No. of patients	AFI	%
15	5.1 – 10 cms (Moderate)	75%
5	≤ 5cms (Severe)	25%
Total (20)		100%

Table-II: Relationship of AFI to IUGR

AFI	No. of cases	Patients of IUGR	%
≤ 5cms	5	5	100%
5.1 – 10 cms	15	9	60%

Table-III: AFI after infusion

AFI	No. of pts. at start	%	No. of pts. at 2 wks	%	No. of pts. at 4 wks	%
≤5cms	5	25%	5	25%	3	15%
5.1-10 cms	15	75%	10	50%	10+2	60%
≥10cms	-	-	5	25%	5	25%
Total	20	100%	20	100%	20	100%

pts. = patients, wks = weeks.

Table-IV AFI and Pregnancy Outcome

AFI	Pregnancy outcome		
	Premature	Normal vaginal delivery	LSCS
<5cms	1 (33.3%)	1 (33.3%)	1 (33.33%)
5.1-10 cms	2 (16.66%)	7 (58.33%)	3 (25.00%)
≥10cms	-	4 (80%)	1 (20%)

Table-V: AFI & Foetal Outcome

AFI	VLBW Baby	LBW Baby	Normal Baby	A/S <5
≤5cms	3 (100%) -	-	8 (66.66%)	4
5.1-10 cms-	-	4 (33.33%)	4 (80%)	3
≥10cms	-	1 (20%)		0

amnios on repeat USG were seen to have improved the AFI to normal after 2 weeks of repeat infusion. However, repeat infusion after 2 weeks was given for maintenance of normal AFI. No appreciable improvement was seen in patients with severe oligohydramnios within 2 weeks only.

Repeat infusion was given after 2 weeks and 2(40%) patients with severe oligohydramnios had improved AFI to moderate level (Table-III). Out of 5 patients with severe oligohydramnios 2(40%) improved to moderate oligohydramnios. Out of the 3 in severe oligohydramnios group 1(33%) underwent LSCS, 1(33%) delivered normally at 36 weeks with moderate oligohydramnios and 1(33%) had premature delivery.

Out of 12 patients in moderate oligohydramnios group, 2(16.6%) had premature delivery, 7(58.33%) had normal delivery around 37 weeks and 3(25%) underwent LSCS for FD and IUGR.

Out of 5 patients, whose liquor improved to AFI >10, 4(80%) delivered normally, whereas 1(20%) underwent LSCS (Table-IV).

Patients with moderate oligohydramnios had 2(16.66%) preterm deliveries, 3(25%) LSCS for FD, muconium and malpresentations.

Out of patients with severe oligohydramnios, 1(33%) had preterm delivery and 1(33%) had LSCS for F.D.

Babies of severe oligohydramnios patients had low A/S and 3(100%) were VLBW (Table-V). Babies of patients whose oligohydramnios improved to normal had good A/S instead of being LBW.

Discussion

Second important cause of IUGR and associated complications is said to be inadequate nutrition to mother [1], . So improving the maternal nutritional status during pregnancy shall improve the pregnancy outcome. Various studies have tried intravenous infusion of large amounts of glucose and aminoacids to the mothers [4]. Mothers carrying IUGR babies have been infused with 10% Fructodex and aminoacid solutions [5]. Pregnant patients with oligohydramnios also have been infused with aminoacids for improvement of foetal outcome [6]. Improved maternal nutritional status by intravenous aminoacid infusion appears to improve the AFI. This improvement may not have been achieved with diet alone because of non-compliance and socio-economic status.

Conclusion

From the study conducted it can be suggested that I/V infusion of aminoacids and Fructodex has a beneficial effect to both mother and foetus in case of idiopathic oligohydramnios in developing countries. However, larger studies with controlled trial are needed to be done.

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Skin Closure with Automatic Stapling in Total Hip and Knee Arthroplasty.

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Abstract.
Effective skin closure conducive to wound healing by primary intention is vital for the postoperative morbidity. Skin closure has proved elusive despite unceasing efforts for many millennia not only due to techniques but also because no ideal suture material has so far been found. We evaluated the results of skin closure with automatic stapling in total hip and knee joint replacements in a series of 182 consecutive hip and knee arthroplasties performed under the care of senior author in our hospital since September 2000. All patients had satisfactory wound healing in our series apart from two minor problems. We haven't come across any other report of skin closure with staples exclusively in relation to arthroplasties to-date in English literature.

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Introduction.

Prevention of infection is of paramount importance in joint replacement surgery which can not be overemphasised. Modern surgical techniques coupled with antibiotic prophylaxis minimise the infection rate.

Objective.

To evaluate the results of skin closure with automatic stapling(single use reflex skin stapler from ConMed corporation, figure 1) in total hip and knee arthroplasty in a series of 182 consecutive total hip and knee arthroplasties since September 2000.

Method.

182 consecutive patients at our hospital under the care of the senior author (AH) underwent arthroplasty of the hip or the knee joint between September 2000 and March 2005. There were 101 males and 81 females. 110 patients had total hip arthroplasty and 72 patients underwent knee replacement. Average age of the patients was 74.3 years.(Range 63-87)

The operations were performed in the standard manner in a laminar flow theatre. Usual preparation of skin with antiseptics and steridrapes was used in all patients. Wounds were closed in layers in all patients and skin closure was done with automatic stapler and occlusive dressing was applied. The dressing was not disturbed in the postoperative period unless there was a problem. Staples were usually removed between 12 14 days and only those with positive wound swabs were regarded as wound infections.

Results.

We encountered no major wound problems (Figure 2 and 3). There was a solitary case of superficial wound infection by MRSA, which settled uneventfully with antibiotics and one patient had a superficial partial wound dehiscence after clip removal at 14 days. The wound was held together with steristrips and healed uneventfully.

Discussion.

Effective skin closure conducive to wound healing by primary intention is vital for the postoperative morbidity. Skin closure has proved elusive despite unceasing efforts for many millennia not only due to techniques but also because no ideal suture material has so far been found.

General classification of sutures include natural and synthetic, absorbable and non-absorbable, monofilament and polyfilament. Synthetic materials cause less reaction and minimize the inflammatory reaction around the suture material. Monofilament sutures have less drag through the tissues and also decrease infection rate unlike braided Polyfilaments which potentially can harbour bacterial inocula.

Staples provide a fast method for wound closure and have been associated with decreased infection rates. Staples are composed of stainless steel and this has been shown to cause less reactive inflammation than traditional suture material. The act of stapling requires minimal skin penetration and thus fewer micro-organisms are carried in to the deeper layers. With proper placement of the staples the resultant scar formation is cosmetically equivalent to that of other techniques. Staples also evade the issue of handling and knot security which is an important feature in selection of any

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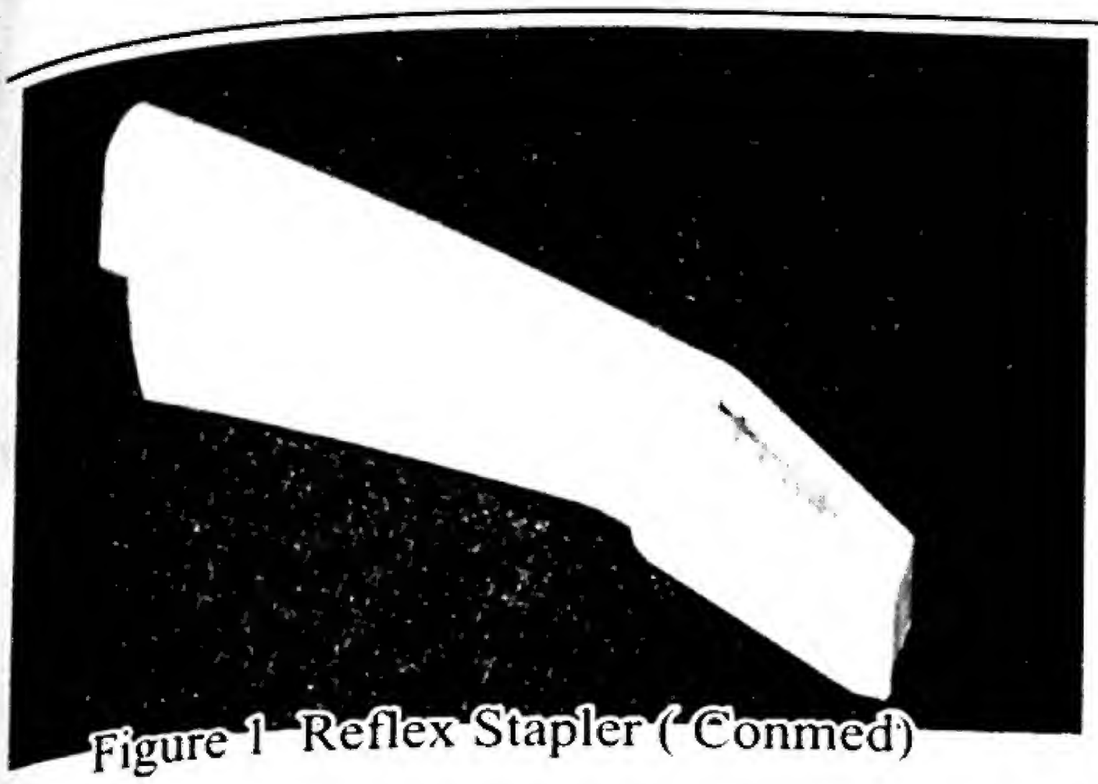

Figure 1 Reflex Stapler (Conmed)

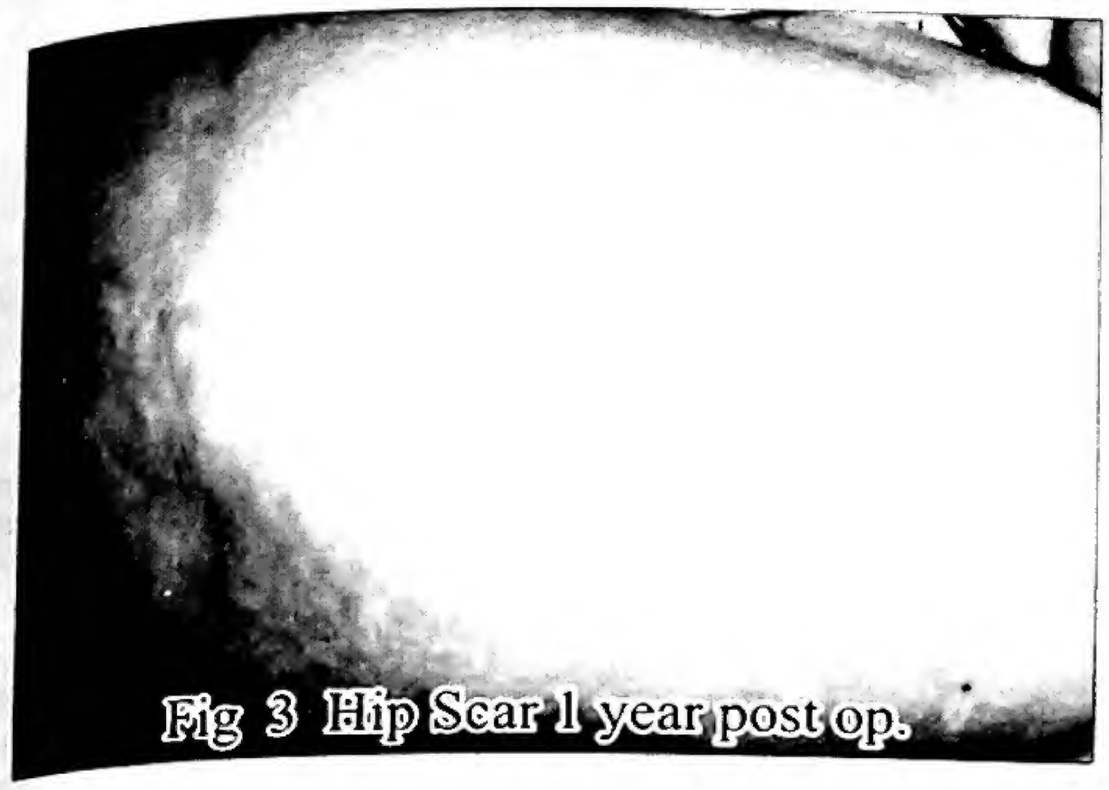

Fig 3 Hip Scar 1 year post op.

Figure 2- Stapled Knee Wound 5th Po Day.

suture material [1]

Choice of suture material and method is not only surgeon and institution dependant, but is also dictated by patient preference, cosmetic and economic analysis.

Stockley, Elson [2] compared staples and nylon and found a higher incidence of inflammation and discomfort on removal of staples. The only advantage was speed of wound closure.

Clayer and Southwood [3] compared skin closure with staples and prolene in hip surgery. They found no significant difference between the two except that staple insertion sites were more obvious in scar that had the staples removed at a later time.

Apart from the above references we haven't come across any other report of skin closure with staples exclusively in relation to arthroplasties to-date.

Conclusion.

Our study represents the first reported series supportive of skin closure with staples in lower limb arthroplasty . Stapling facilitates rapid closure of skin and saves the surgeon from the risk of needle stick injury. In our experience it provides the patient with excellent wound healing.

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Spontaneous CSF Rhinorrhoea-A Rare Complication of Pseudotumor Cerebri

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Abstract:

Pseudotumor Cerebri (also known as benign intracranial hypertension) is a syndrome characterized by headache, papilledema, minimal or absent focal neurological signs and normal CSF composition in the absence of an intracranial mass or dilated ventricles on CT or MRI. Pseudotomor cerebri has number of causes (e.g dural sinus thrombosis, chronic meningitis, drugs etc.) in which case it is called as secondary pseudotumor syndrome. The most common form, called as idiopathic intracranial hypertension , has no established cause. Spontaneous CSF rhinorrhea is a rare complication of this syndrome.

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Case Report:

An elderly female patient presented to the medical OPD of SMHS Hospital Srinagar with complaints of chronic headache ; she was a known hypertensive with type II diabetes mellitus which were well controlled. Her fundus examination revealed bilateral papilledema and as such, the patient was referred for MR imaging. MRI revealed a partially empty enlarged sella with dilation and tortuosity of optic nerve sheaths , distension of optic nerve sheath and mild flattening of globes at optic nerve insertion . There was no evidence of dural sinus thrombosis or meningeal enhancement . The MR findings were interpreted as being consistent with the diagnosis of idiopathic intracranial hypertension. The patient was put on acetazolamide and gradually became symptomatically better. However, after a year the patient noticed watery nasal discharge which was exacerbated by stooping forward and was confined to right nostril. Initially, it was interpreted as allergic rhinitis and the patient was given symptomatic treatment with nasal decongestants without any relief. Later CSF rhinorhoea was suspected and patient was referred to the Department of Radiodiagnosis for MRI. The coronal FLAIR and T2 W images revealed a small meningocele protruding through cribriform plate into the superior nasal cavity (Fig.1). The optic nerve sheaths were dilated with empty enlarged sella (consistent with her earlier diagnosis of pseudotumor cerebri). CT cisternography was performed after injecting 10ml of water soluble non ionic contrast (iohexol) and performing 2mm coronal slices in the suspect region as revealed by MRI. A small bone defect was noticed in the right cribriform plate with the contrast filling the anterior ethmoid air cells and a tiny meningocele. Contrast accumulated in the cotton pledget put in the right nares (Fig 2&3). The patient underwent a successful endoscopic repair of the defect with sealing of the leak using tensor fascia lata graft. The patient is on regular follow up and is asymptomatic since then

Discussion:

Clarke et al described 4 cases of pseudotumor with the complication of CSF rhinorrhea ; all patients were in the age range of 33 to 44 years on treatment from 8 months to 11 years. Cribriform plate was the site of leak in all patients [1].Dunn CJ et al reviewed 15 patients with spontaneous CSF rhinorrhoea . 14 patients were elderly females (37-70 yrs); all female patients were overweight with a body mass index (BMI) greater than 24.9 , 9 patients were obese with BMI more than 30 [2] . Schlosser et al studied sixteen patients with spontaneous CSF leaks and found that 10 had completely empty sella and 5 had partially empty sella . They concluded that empty sella represents a sign of increased intracranial pressure that leads to spontaneous csf leak ; interestingly 13 of the sixteen patients were obese , middle aged females [3]. Tolley NS in their study of 10 patients with spontaneous CSF rhinorrhoea observed that the site of fistula could be radiologically identified in 90 per cent of cases . Precontrast bony dehiscences were identified in all patients leaking from cribriform plate region , but contrast CT was better in confirming the leak . These authors also noted deviation of crista galli in patients leaking from cribriform plate region [4]. Johnson DB et al studied 24 patients using MRI, nine of them were not actively leaking at the time of scanning . The site

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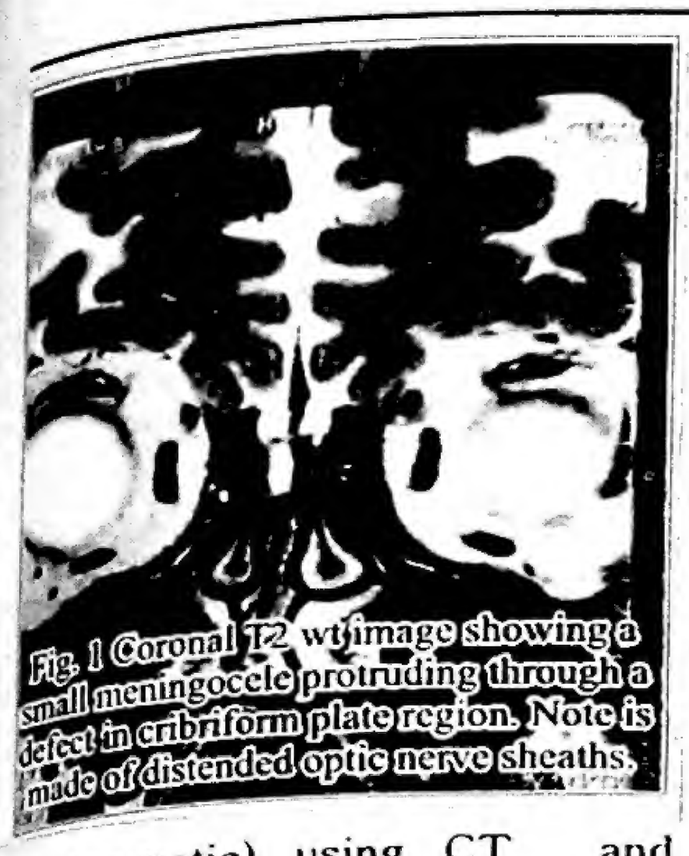
Fig. 1 Coronal T2 wt image showing a small meningocele protruding through a defect in cribriform plate region. Note is made of distended optic nerve sheaths.

of CSF leak was identified in all 24 patients using MRI, and was subsequently verified at operation [5]. Levy LM et al in a similar study of 7 patients found flow sensitive MRI useful for identification of CSF leaks[6]. Wakhloo AK et al studied 16 patients with CSF leak (traumatic and nontraumatic) using CT and digital subtraction cisternography and found the latter most sensitive for diagnosing dural and bony defects. They also employed MRI using heavily weighted T2 images (a modification of rapid acquisition with relaxation enhancement) in 6 cases, which demonstrated the fistula in 4 patints [7]. Tuntiyatorn L evaluated MR cisternography using heavily T2 wt fast spin echo sequences in 35 patients with CSF leaks, employing additional plain HRCT in some cases Criteria for positive results were demonstrable fistular tract connecting subarachnoid space to paranasal sinus or petrous bone , dural discontinuity, bone defect with pneumoencephalus, and presence of brain herniation . It was concluded that combination of MR cisternography and plain HRCT are highly accurate in locating the site and extent of CSF fistula [8].

Idiopathic intracranial hypertension typically affects obese females in 20-44 year age group of the 19/100000 the main symptoms are headache (which is episodic, throbbing and aggravated by valsalva), blurred vision, minimal horizontal diplopia and transient visual obscuration. The CSF pressure is elevated (150 to 450 mm H20) with periodically occurring plateau waves of increasing pressure lasting 20 to 30 min. The main consideration in such cases is to distinguish idiopathic pseudotumor cerebri from secondary pseudotumor syndrome secondary to dural venous sinus thrombosis, gliomatosis cerebri, occult AV malformation, carcinomatous, infectious or granulomatous meningitis . MRI findings reveal enlarged optic nerve sheaths (best seen on T2 Wt. coronal images) with flattening of globes at optic nerve insertion (best seen on axial images) in 40-50% of patients. In severe cases, the optic nerve papillae may protrude into the globes; this finding may reverse after successful medical or surgical treatment. Diffusion weighted images reveal normal brain water diffusion and proton longitudinal relaxation time. MR venogram by demonstrating dural occlusion, and contrast enhanced MRI by showing abnormal meningeal enhancement, can help in differentiating idiopathic from secondary pseudotumor syndrome.[9].

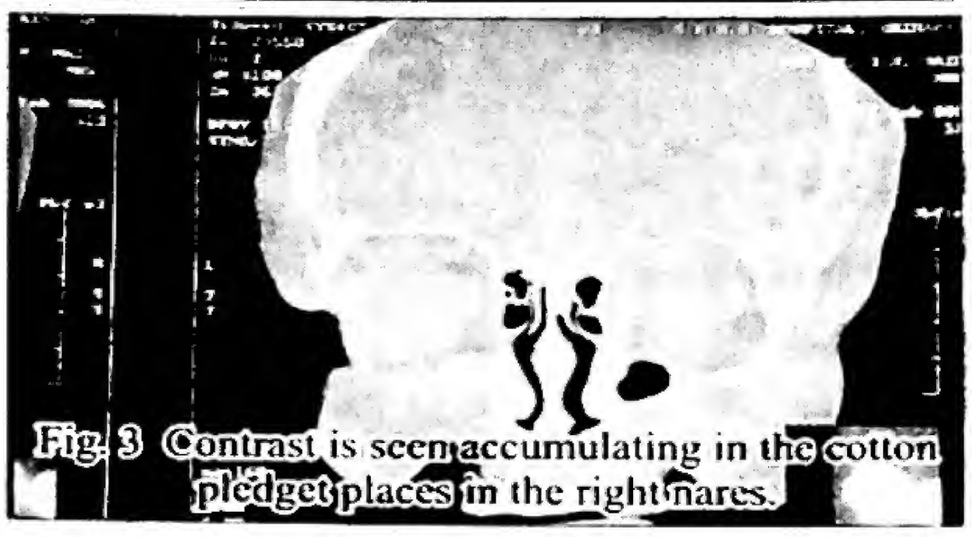
Fig. 3 Contrast is seen accumulating in the cotton pledget places in the right nares.

Spontaneous CSF leak is a rare complication of pseudotumor cerebri [1,3]. The role of imaging is to identify the site of the leak before an operative repair is undertaken, and to identify other causes of spontaneous CSF leaks which include fontoethmidal meningocele and congenital bone defects. The various imaging modalities include radionuclide cisternography using indium 111, coronal high resolution T2 and FLAIR MRI and HRCT-Myelography. In our case the leak was initially demonstrated by MRI and subsequently verified by CT Myelography. The latter technique can define the bone defects; however, intrathecal administration of contrast is needed for definitive demonstration of CSF leak.Endoscopic closure of dural defects is the treatment of choice [10].

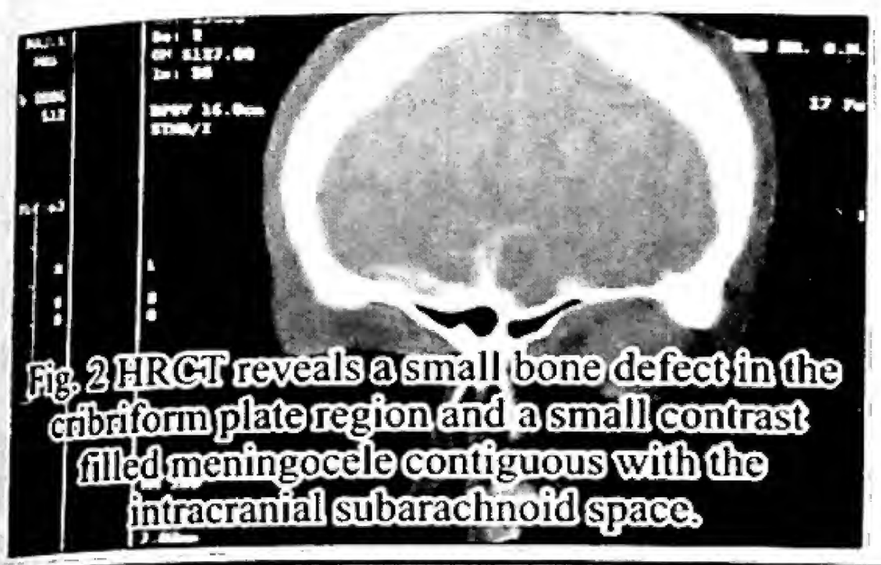
Fig. 2 HRCT reveals a small bone defect in the cribriform plate region and a small contrast filled meningocele contiguous with the intracranial subarachnoid space.

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Kawasaki disease: Unusual presentation in a three year old girl with a short review.

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ABSTRACT

Kawasaki Disease (KD) is consistently now being recognized as a disease in children, and because of unusual manifestations it is overlooked as a clinical entity. KD is usually characterized by fever, rash, swelling of the hands and feet, irritation and redness of the conjunctiva, swollen lymph glands in the neck, and irritation and inflammation of the mouth, lips, and throat. We here report an unusual presentation of KD in a three year old girl having hepatitis and febrile convulsions as predominant features, rather than the usual vasculitic manifestations. This girl presented with pyrexial illness (high grade), dysuria and characteristic rash, consistent with KD. The child also had edema of limbs and urinary symptoms.

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CASE REPORT

A previously well 3 yr old girl presented with one month history of dysuria, oliguria and redness with pain around urethra. She also had high grade fever and two episodes of convulsions. Three weeks after the start of illness, the parents noticed eruption of rash, which started on the trunk first and later involved rest of the body, including the limbs. It was non-itchy and of exfoliative type. This was accompanied with reddening and exudation from oral mucosa and lips. Along with the rash, parents also noticed yellowing of the sclerae which gradually deepened.

There was no recent history of: intake of ampicillin, sore throat or arthritis. There were no prodromal symptoms suggestive of measles. Further, there was no history of a similar illness in the past and other children in the family were in good health. On examination the child was irritable, with a high grade fever (40°C). She had yellowish discoloration of her sclerae, fissured and excoriated lips *(Fig. 1)*, and injected oral mucosa. Tongue was normal and there was submandibular lymphadenopathy (2cm) on the left side. There was also a pitting edema of the upper and lower limbs. There was no induration at the site of the BCG mark. The whole body, esp. the trunk had a morbilliform rash, which was extending to the limbs *(Fig. 2)*. Abdominal examination revealed mild hepatomegaly, rest of the systemic examination being normal. A clinical diagnosis of KD was made and patient was admitted. Investigations revealed Hb:9.6gm/dl, TLC:12000/mm^3, DLC:P 32% and L 58%, Platelet count:2.5x10^5, CRP:192 mg/dl. PT:22sec, aPTT:31sec. PBF showed microcytic hypochromic anemia, with no atypical lymphocytes. Urine examination revealed 10-20 leucocytes/HPF, 1-2 RBCs, Crystals++ and traces of Albumin. Liver enzymes were elevated: Aspartate aminotransferase (AST):310U/L, ALT (Alanine aminotransferases):395U/L, ALP (Alkaline phosphatase):1159U/L. Bilirubin initially was 4.8mg/dl and few days later rose to 13.6mg/dl. Serum was negative for IgM Anti HAV, HBsAg, Anti HCV, and IgM Anti HEV, ASO, ANA and RF. Monospot Test for Infectious Mononucleosis was also negative. Chest X Ray was normal. Ultrasonography (USG) abdomen revealed mild hepatomegaly with a normal gallbladder. Echocardiography(ECHO) was normal except for a mild pericardial effusion. Electrocardiography(ECG) was also normal.

The patient was put on high dose i.v. fluids and Cefatoxime. Hepatitis was managed conservatively. She could not be given aspirin due to elevated aminotransferases also Intravenous Immunoglobulins (IVIGs) were not given due to non affordability on part of the attendants. Two days after presentation the edema got spontaneously resolved. The rash continued for another week when it was gradually replaced by desquamation of skin all over the body. Three weeks after admission her icterus regressed, rash had completely disappeared, exfoliation of skin decreased gradually and she was discharged from the hospital. On follow up, five months later, she was in good health.

DISCUSSION

Kawasaki disease (KD) is an acute multisystem vasculitic syndrome of unknown etiology that occurs in infants and children younger than 5 years of age[1,2] The disease has now surpassed acute rheumatic fever as the leading cause of acquired heart disease in children [3,4] KD occurs worldwide, with incidence of 9 to 19 per 100,000 in children younger than 5 years of age. Peak incidence is reported in children aged 9-11 months [5] There being no specific test for KD, its diagnosis is based on clinical criteria alone, with exclusion of other diseases (*Table 1*).

KD may present in two ways:

(A) Complete cases: these include fever of five days duration plus 4 of 5 remaining

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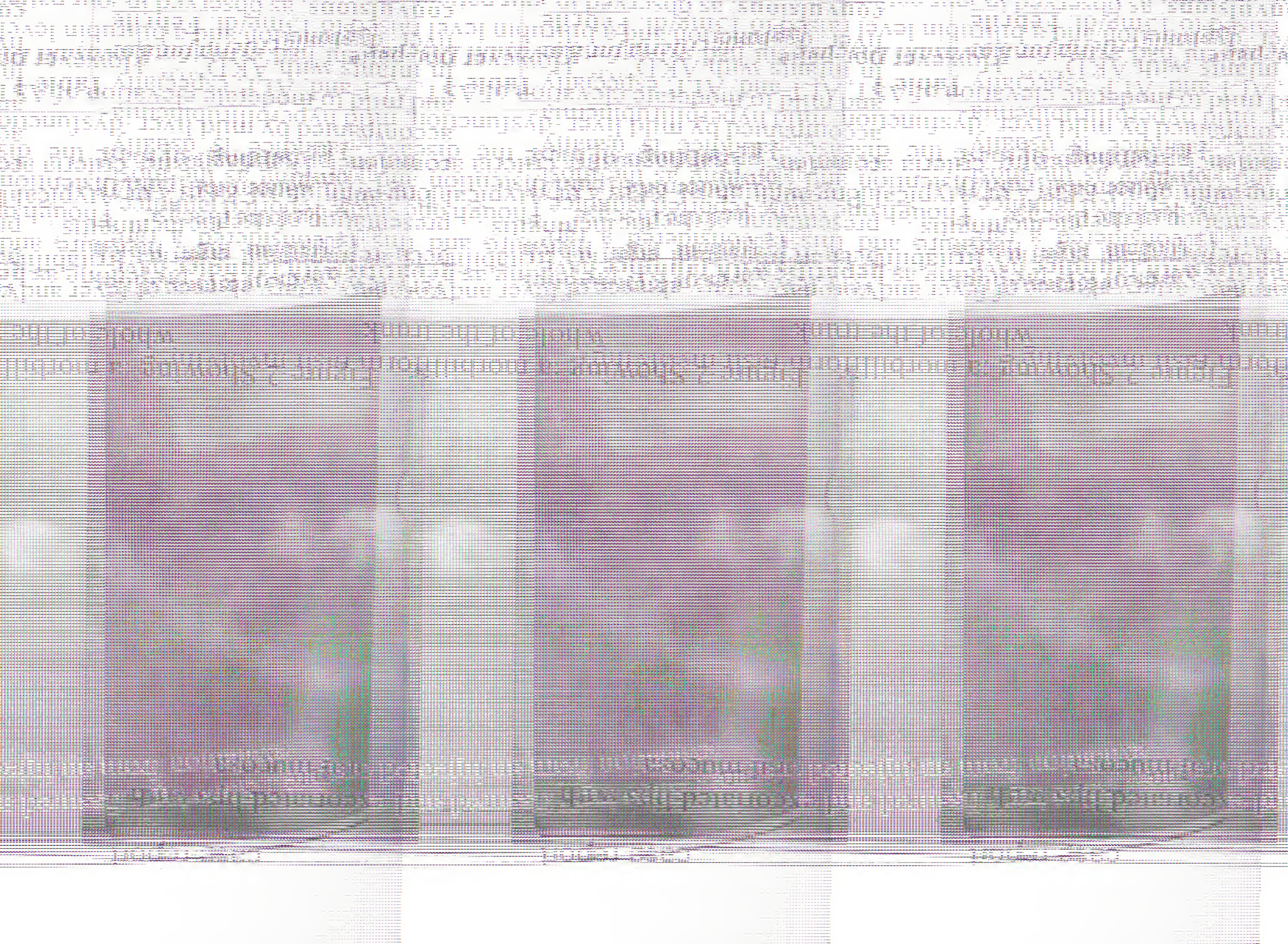

Benign acute childhood myositis; presentation and management in emergency

Wajid Ali, Mushtaq Ahmad Bhat, Parvez Ahmad

ABSTRACT
Benign childhood myositis is an uncommon disorder in the pediatric population. It usually follows an upper respiratory illness especially by influenza B virus and has a benign course with spontaneous recovery. We present three cases of such an illness with review of literature

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Introduction

Viral infections are an important causes of respiratory tract disease in the childhood [1].The spectrum of clinical manifestations is wide, ranging from mild upper respiratory illness to bronchiolitis and pneumonia [2].However the commonest presentation in children is fever, cough and headache. Benign acute childhood myositis is especially seen with influenza virus [3-12].It usually occurs in the acute convalescent phase of typical influenza infection. There is sudden pain and tenderness in both calves with difficulty in walking associated with characteristic rise in creatinine kinase and aspartate aminotransferase. The purpose of this study was to present the clinical scenario and management of pediatric patients presenting with benign childhood myositis.

CASE 1

A 5 year old boy presented with a three day history of fever and headache, followed by a 24 hour history of painful calves. He first experienced the pain during middle of the night and had progressive difficulty in walking. On examination he had coryza and had palpable cervical lymph nodes. Both calves were tender but no swelling, erythema, or wasting was noted. His urine dipstick for myoglobinuria was negative. He had normal counts and erythrocyte sedimentation rate (ESR) was normal. His creatinine phosphokinase (CPK) and aspartate aminotransferase (AST) were raised (see table 1).He was discharged and became asymptomatic within 72 hours. CPK had returned to normal within two weeks.

CASE 2

An eight year old boy attended with a two day history of headache, sore throat, anorexia, and pyrexia. Two days after this resolved he woke up with painful calves. On examination he was apyrexial, had enlarged tonsils, and palpable cervical lymph nodes. He had tender calves but no evidence of swelling or erythema. His urine dipstick was normal. He had a mild leucopenia, borderline platelets, but a normal ESR. His CPK and AST was moderately elevated (see table 1) He was discharged home and became asymptomatic 48 hours after discharge. When he attended review clinic two weeks later his CPK had returned to normal.

CASE 3

A 6 year old boy presented with a four days history of headache, coryza, and cough. He developed calf pain on day 3. On examination he was apyrexial and had no palpable lymph nodes. He had tender calves and was walking with extended legs and a broad based gait. His neurological examination revealed no evidence of pathology. His feet were cold but capillary return was less than two seconds. He had mild leucopenia, borderline low platelets, but a normal ESR. His CPK was very elevated (see table 1).He was asymptomatic when seen in clinic ten days later and his CPK had returned to normal

DISCUSSION

In 1957 Lundberg published the first report of "myalgia cruris epidemica [1] which was a newly identified syndrome of muscle pain, predominantly affecting the calves and occurring in school age children. The condition followed a prodrome of febrile illness, striking in the first few months of the year. The patients were typically boys, many of whom reported participating in strenuous activity before the onset of pain. All children recovered within a week. Lundberg felt that in view of the well described prodrome, the accumulation of cases within families and schools, in addition to leucopenia and increased sedimentation demonstrated in affected patients, the etiological agent was likely to be a virus.

Since then various descriptions have been given to the disorder and despite some debate about the actual muscle pathology, the term myositis seems to be generally used. This is a reflection of the assumption that there must be at least an element of muscle inflammation to account for the release of CPK. Many authors have

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termedthe syndrome benign acute childhood myositis (BACM).

It is interesting to note that two of our patients had

Table1.Blood results

Cases	WBC (x10³)	Platelets	CPK	AST
1.	4.2	230	1860	420
2.	2.8	150	1700	380
3.	3.4	160	1200	268

unusually cold feet—a sign which, to the best of our knowledge, has not been associated with BACM previously. This may suggest the pathogenesis involves a vascular component although in both these children the capillary return was normal.

The majority of reports have associated the illness with influenza viruses, particularly influenza B [3,4, 7-9, 11]. All the three children had evidence of recent influenza B infection and there was evidence of significant influenza B activity in the community at the time our cases presented [12].

It has been suggested that susceptible children only become ill on the primary exposure to a particular strain of influenza, which may account for the lack of cases seen in adults. It has been shown from serological testing that children with myositis in association with influenza were naïve to the infecting strain [3,7]. Two children have been recorded as developing a second episode of myositis in response to a different strain of influenza, but when re-exposed to a previously encountered strain did not develop myositis [7].

Some authors have not derived any association with influenzaeither in terms of virus isolation or serology [5,6] Although this could be the result of inadequate sampling or laboratory techniques, it seems that other viruses may also cause an indistinguishable syndrome. Indeed, more recently adenovirus, [9] HSV, [8] and EBV [10] have been found in association with BACM.

Despite lack of evidence for the same viral agent it is difficult to ignore that all our cases presented within a few days with an almost identical clinical picture. All of our children had serology suggestive of recent infections and virus cultures are pending, these are common pathogens and may have been coincidental to their myositis presentation. It is conceivable that a single undetected viral agent was responsible for all of the children's illnesses. Surprisingly, none of our patients lived in neighboring areas and all went to different schools.

MANAGEMENT

A large number of conditions can cause muscle pain in children and it is important to distinguish BACM from other more severe illnesses.

Firstly the history is generally consistent: a viral prodrome followed by acute onset of severe muscle pain, usually confined to the legs. The resolution of symptoms is swift—many patients are markedly improved within 24 hours. A full and thorough examination should be performed to include a detailed neurological examination. Neurological signs otherthan weakness as a result of muscle pain may herald more severe pathology. The most consistent laboratory result is a raised CPK but it is important to rule out rhabdomyolysis by performing urinalysis for evidence of myoglobin. It is prudent if drawing blood to perform a full blood count, basic biochemistry, and send a serum sample to virology.

If the presentation is of classical BACM then the pediatrician should feel comfortable discharging the patient. However the patient should be reviewed after a couple of days to ensure complete resolution of symptoms. At this stage it would be useful from an epidemiological point of view to draw blood for convalescent viral titres.

CONCLUSION

It is important to recognize BACM as a self-limiting condition which could however be mistaken for a more sinister disease and unnecessary tests instigated. As clusters of cases occur, children are likely to self present to emergency because the symptoms are alarming. However the syndrome can be managed safely in an emergency setting. In highlighting this condition it may be that more thorough viral studies are performed in future cases, to understand the infective etiology of this syndrome.

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Acardiac Twin

Syeed Masuma Rizvi, Farhat Jabeen

Here we report case of rare anomaly.[1] A third gravida lady with one normal delivery and one abortion was admitted in the hospital as a case of retained second twin. First of the twins was delivered at home, born died. She reported to hospital after twelve hours of the first delivery. All means of medical induction tried without achieving successful cervical dilation. Caesarian section was planned. An acardiac twin with complete malformation of upper torso was delivered with great difficulty.

More etal (1900)[2] have described the outcome of 49 pregnancies complicated by acardiac twining. Quintero etal (1994)[3] reviewed methods of in utero treatment of acardiac twining where the aim is interruption of vascular communication between the pump and the recipient twin. They also described successful use of transabdominal fetoscopy to ligate the umbilical cord of 11 acardiac twins.

In our case, the patient reported quite late with one of the twins having been delivered at home, born dead. Diagnosis of acardic twin continues to prove a problem[4].The ultrasonographic features of absent head and trunk regions and increased soft tissue in the body aid in correct diagnosis.[5]

Innovation in management, pharmacologic treatment of the pump twin, or surgical interruption of acardiac umbilical flow may alter the prognosis in selective cases[2].

Insertion of a helical metal coil to induce thrombosis in the umbilical artery of the acardiac twin is a noval approach to save the co-twin[6].

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Package inserts-do they have any role ?

Bansal V, Dhamija P, MedhiB, Pandhi P.

ABSTRACT

Introduction: Package insert is an essential feature of drug packaging. Often unread they have potential educational and legal implications[1]. The inserts available today are mostly physician oriented. This has partially marginalized their utility for common man.To identify the awareness and deficiency in drug label. A set of questions was prepared for medical personnel (i.e resident doctors and nurses of PGIMER, Chandigarh) and patients/attendants.300 proformas(100 each) were circulated among them after explaining the nature of study. The responses were marked as agree/disagree/no comments. Results were expressed as percentage of total responses for that question. Majority of the respondents believed to know the importance of package inserts. General agreement for relevance of information. Opinion was against adequate mentioning of negative points, references quoting and regular updating. Small font size was a common problem. A lot needs to be done to make package inserts more reader friendly and enhance their utility. With more stringent rules for regulating the contents and references, their quality can be improved.

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INTRODUCTION

Package insert or product label is an essential feature of drug packaging[1]. These inserts are present in most of the medicinal and pharmaceutical products as a piece of paper with information pertaining to that particular product. Ethically and legally speaking they should provide all the necessary information of the drugs in correct and easily understandable form for safe and effective use[2]. The information should be unbiased, should not hide anything and regularly updated. Often unread they have potential educational and even legal implications. However, it is often noticed that for most of the individuals these papers are as if non existent, and just another promotional advertisement. Most are perhaps ignorant about the information that these papers may carry which even their physicians may not be knowing or they didn't have time to tell their patients. The study was planned to look into the awareness in the common public besides medical fraternity about these small pieces of papers whose accuracy is a big liability for the pharmaceuticals.

MATERIALS AND METHODS

A set of questions was prepared for medical personnel (i.e. resident doctors and nurses of PGIMER, Chandigarh) and patients or their attendants. One hundred performs each were circulated among resident doctors, nurses and patients/attendants after explaining them the nature of study. Resident doctors attending the outpatient department of PGIMER, Chandigarh were given the proformas and requested to fill them up in their free time. They were then collected at a later date depending upon their availability. The proformas were circulated and filled by the nursing students and staff of National Institute of Nursing Education, PGIMER. Patients attending the outpatient department of PGIMER were approached at random and were requested to fill up these. Those who were not able to fill up these proformas individually were helped by their attendants for the same. The responses were marked as agree/disagree/no comments. Filled proformas were collected. Data was compiled and analysed. Results were expressed as percentage of total responses for that question.

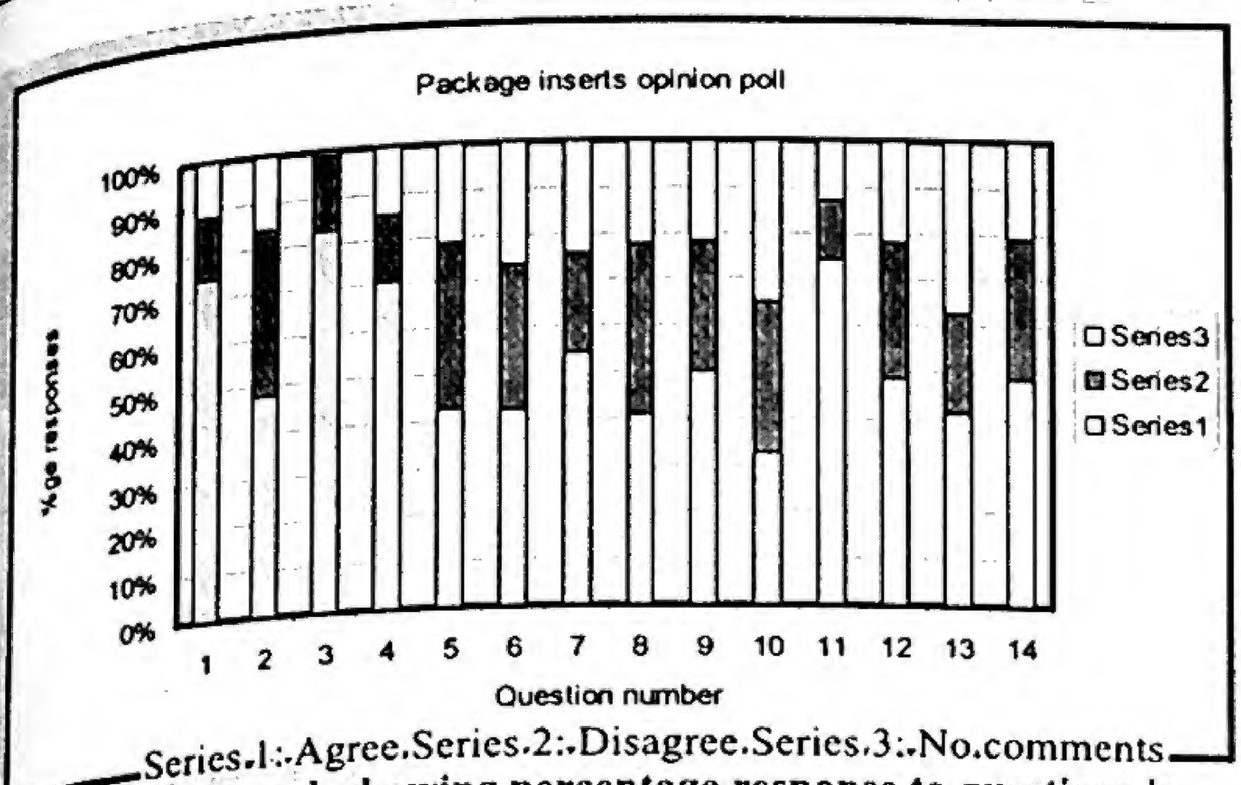
RESULTS

Majority of the respondents knew the importance of package inserts. Majority agreed that the information given is relevant and not biased about the product, but the inserts did not mention all the negative points of the product. Opinion was divided equally about the use of language and terminology in the package inserts. Majority of the respondents believed that the references quoted were not dependable and the constant revision of the insets. Significant number of the respondents was not aware about the guidelines for regulating the contents of inserts. Finally small font size was a common problem for most of the subjects.

Questionnaire:

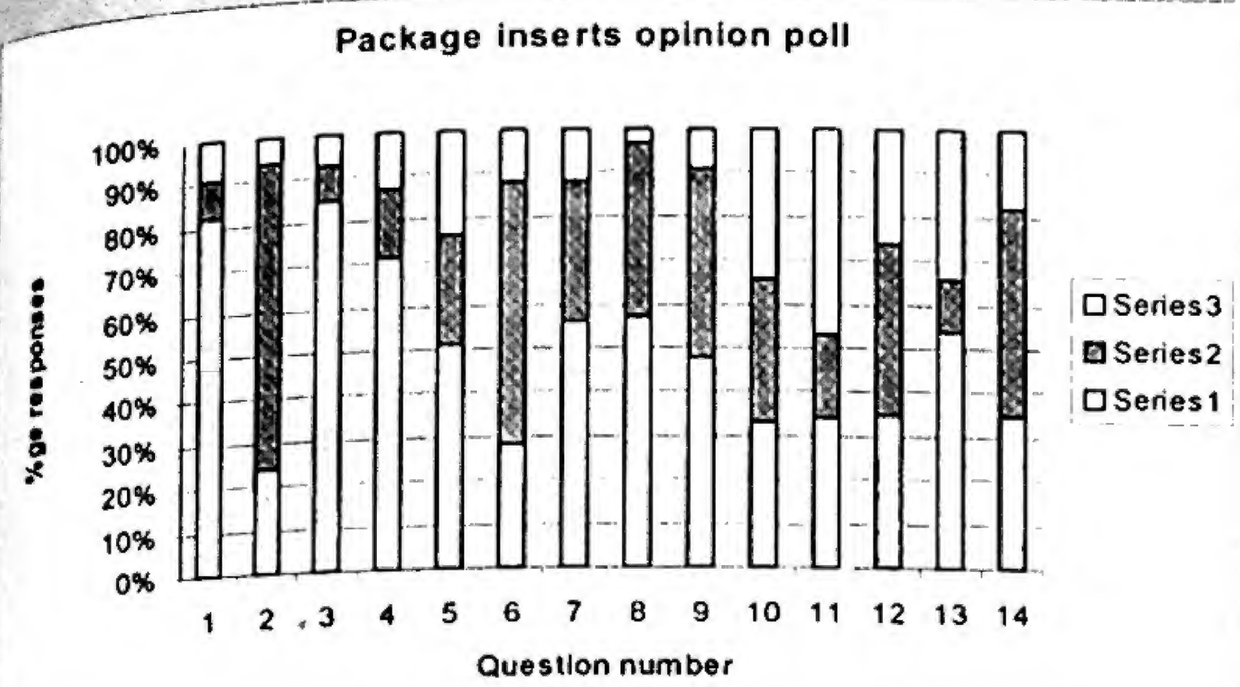
1. Do you know the relevance of paper/package insert?
2. Is reading package inserts time consuming?
3. Do the package inserts give relevant information?
4. Is the information based on priorities?
5. Is the information biased i.e favors the product?

Keywords: Package inserts, relevance



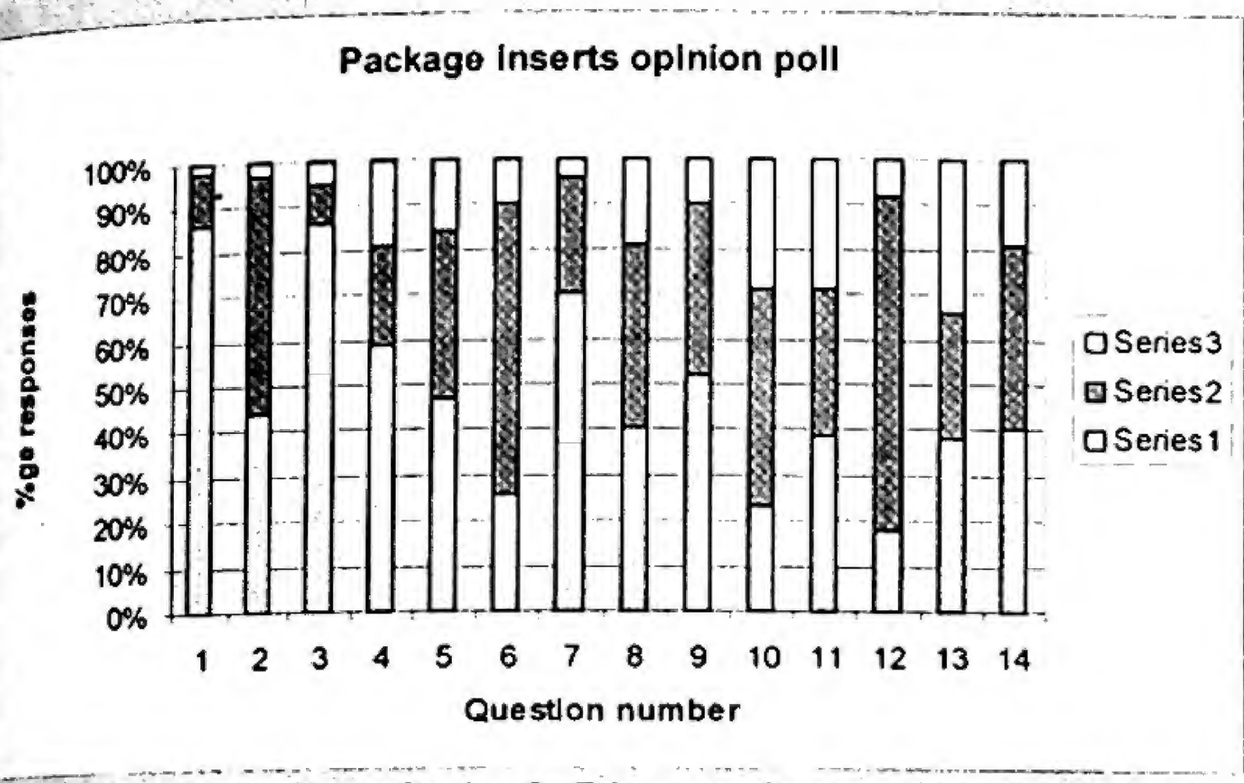
Series.1:.Agree.Series.2:.Disagree.Series.3:.No.comments

Figure 1: Graph showing percentage response to questions in patient/attendant arm



Series 1: Agree Series 2: Disagree Series 3: No comments

Figure 2: Graph showing percentage response to questions in nurses arm.



Series 1: Agree Series 2: Disagree Series 3; No comments

Figure 3: Graph showing percentage responses to questions in resident doctor's arm

6. Are all the negative points of the productillustrated?
7. Is the font size or size of alphabets too small for comfortable reading?
8. Is there too much use of medical terminology in package inserts?
9. Do you find some language barrier for comprehension of the inserts?
10. Do you think the reference sources are dependable?
11. Do you think package inserts are regularly updated with new information?
12. Do you find inserts merely as an advertisement?
13. Do you think guidelines for contents of package inserts are strict enough?
14. Do you think that these inserts can cause confusion in the patients?

DISCUSSION

Package insert is a legally required document/ label within the package that is intended to inform the user of the approved and off label use of the drug, its dose and any contraindications or side effects a drug may have[1].

There is a mismatch in the information that a package insert should provide and information that a package insert actually provides. Whatsoever information is there, significant disagreement exists over that like bias favouring product, lack of evidence supporting data. Even use of medical terminology and small font size lead to non usage of package inserts.

If we see the contents of package insert of developed countries, the quality control and product information provided in them, there is a gross difference. Approval by regulating agencies, regular upgrading by the pharmaceuticals and patient awareness to read and comply with the information provided tells the necessity to have a good package insert.

Clear and comprehensible labeling of a drug product is essential for establishing appropriate use among patients and thereby maintaining safety and optimizing efficacy and compliance. The labeling must be able to convey the intended use of the product, provide adequate directions for its use, warn against potential harmful effects and provide instructions for appropriate length of treatment and when to seek medical advice[4]. These labels should be prepared keeping in mind the general level of understanding and educational status of common man. Pharmacokinetic and pharmacodynamic data should be neatly and clearly mentioned along with indications for which they are used. Clear cut mention for evidence of off label uses of drugs should be cited. Signs and symptoms of drug overuse, their management and indication to visit the physician should be mentioned. In one of the studies of package insert of intrauterine contraceptive devices, the big booklet (about 12 pages) received strong affirmative response with respect to its importance as a source or as a sole source of information than shorter booklet[5].

A few countries have even introduced the concept of electronic package inserts. The pharmacy houses are electronically linked to Central Drug information units which are regularly upgraded regarding drug information. The patient buying a drug is given recently upgraded package insert in print form. It should be clear that these package inserts should only serve as complementary to physicians and pharmacists and should not replace them[1,6].

With OTC status of many drugs available in the market. It is all the more important to prepare good package inserts for the benefit of the society. Under Section 9 (b) of the Indian act, a drug is considered to be misbranded if it is not labeled in the prescribed manner and if the label or container or anything accompanying the drug bears any statement, which makes any claims for the drug, which is false or misleading.

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Autoinduction of Carbamazepine in Indian Paediatric Patients of Epilepsy

Archana Parihar, Rashmi Sharma, Kamlesh Samotra, S.K. Gupta, Bhuvneshwar Kapoor

ABSTRACT

Carbamazepine (CBZ) is one of the most commonly prescribed drugs for epilepsy and the influence of genetic difference, age, sex and race on the blood levels of CBZ and its metabolites is well known. The present study was conducted to study the phenomenon of autoinduction by CBZ in Indian paediatric (< 18 years) patients of epilepsy. Each patient was put on CBZ 15 mg/kg/day and plasma level of CBZ was estimated 4 hours after ingestion of the dose at 0, 2, 3, 4, 6, and 8 weeks. The average plasma concentration of CBZ was 13.93, 12.14, 11.85, 10.42, 9.95 and 9.93 mg/ml at 0, 2, 3, 4, 6 and 8 weeks respectively. Significant reduction in serum CBZ levels as compared to the baseline was observed at 2, 3, 4, 6 and 8 weeks. Maximum autoinduction was seen at 6 weeks (with $P < 0.05$) and remained constant till 8 weeks. The results of our study clearly indicated that CBZ increases its metabolism before 2 weeks of treatment and continues to do so till 6 weeks in Indian paediatric patients. Thus a single CBZ plasma concentration estimation in the start of the study does not serve a basis for predicting steady state concentration.

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INTRODUCTION

Carbamazepine (CBZ) is one of the most commonly prescribed drugs for epilepsy and is also widely used in the treatment of trigeminal neuralgia and psychiatric disorders like mania (bipolar disorder)[1]. It is well absorbed orally with a narrow therapeutic range (4 to 12 mg/ml)[2]. Hence plasma CBZ concentration monitoring is becoming to be used in a more thoughtful critical manner. As CBZ is a drug which induces its own metabolism and can lead to pronounced alteration in its kinetics during chronic treatment[3]. The influence of genetic difference, age, sex and race on the blood levels of CBZ and its metabolites is well known[4]. Although, a few studies are available demonstrating the autoinduction with CBZ in western population[2,3,1], but there is a need to study this aspect of its pharmacokinetics in Indian patients of different age groups with different genetic composition. Hence, the present study was conducted to study the phenomenon of autoinduction by CBZ in Indian paediatric (< 18 years) patients of epilepsy.

MATERIAL & METHODS

This prospective pharmacokinetic study was conducted in the Postgraduate Department of Pharmacology and Therapeutics, Government Medical College, Jammu. Thirteen newly diagnosed paediatric cases of epilepsy attending Neurology Outpatient Department (OPD) of Medicine, Government Medical College, Jammu were included in the study after taking well informed consent from the parents of the patients. During preinclusion visit all patients had to undergo complete physical and systemic examination, haematological investigations (Hb, TLC, DLC, ESR), biochemical investigations (RFT, LFT), ECG and X–ray chest. Patients with any hepatic or renal disease, cardiovascular disease, bone marrow depression, intermittent porphyria, haematological disorders or on any other concomitant therapy, alcoholics and smokers were excluded from the study. Each patient was followed for 8 weeks. After clinical examination and their basic investigations each patient was put on CBZ 15 mg/kg/day. 2ml of blood samples of each patient was taken at 0, 2, 3, 4, 6 and 8 weeks. Each sample was collected 4 hours after ingestion of the drug to estimate the peak levels of CBZ, as peak plasma concentration of CBZ can be reached at about 4–8 hours after oral ingestion[5].

CBZ level estimation was done by using CEDIA Carbamazepine II Assay kit with the help of semiautomatic analyzer (ERBA CHEM PRO)[6].

The assay is based on the bacterial enzyme β galactosidase, which has been genetically engineered into two inactive fragments. These fragments spontaneously reassociate to form fully active enzyme that, in the assay format, cleaves a substrate, generating a colour change that can be measured spectrophotometrically[6].

STATISTICAL ANALYSIS

Plasma levels of CBZ were expressed in mean ± S.D. Levels of the serum CBZ were compared at 0, 2, 3, 4, 6 and 8 weeks using paired 't' test. P value < 0.05 was considered statistically significant. Analysis of Variance (ANOVA) were used to compare plasma levels of CBZ at different weeks.

RESULTS

The average plasma concentration of CBZ was 13.93, 12.14, 11.85, 10.42,

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Keywords: Carbamazepine, Autoinduction, Plasma concentration

TABLE 1: PATIENTS CHARACTERISTICS

Parameters	Observations
Number of patients (*n*)	13
Age (yrs) Mean ± SD	10 ± 2.6
Weight (kg) Mean ± SD	28 ± 7.8
Male : Female	8 : 5
SD = Standard Deviation	

9.95 and 9.93 µg/ml at 0, 2, 3, 4, 6 and 8 weeks respectively. Significant reduction in serum CBZ levels as compared to the baseline was observed at 2, 3, 4, 6 and 8 weeks. Maximum autoinduction was seen at 6 weeks (with $P < 0.05$) and remained constant till 8 weeks.

DISCUSSION

In our study autoinduction of CBZ started at 2 weeks and was maximum at 6 weeks and remained stable till 8 weeks. A significant difference was reported in the plasma levels between 2 and 6 or 8 weeks ($P = 0.0002$).

An earlier study conducted by Bertilsson L et al. (1980), in 3 children in Sweden demonstrated maximum autoinduction by 32 days[7].

Eichelbaum M et al. (1985) demonstrated decreased $t_{1/2}$ and increased total plasma clearance after 6 months of CBZ therapy as compared to single dose studies; further indicating autoinduction with CBZ[8].

In contrast to our study Mikati MA et al. (1989), determined CBZ clearance values in 17 patients at the end of weeks 1, 2, 4, 8 and 12 of monotherapy and found that CBZ autoinduction was completed within the first 1 or 2 weeks of monotherapy[9].

However, in agreement with our study Bernus I et al. (1994) studied pharmacokinetics of CBZ in 6 healthy young adult male volunteers who were given two 600 mg oral doses of CBZ 5 days apart. The pharmacokinetic analysis showed that autoinduction of CBZ metabolism was present within 6–10 days of the initial drug dose[10].

The results of our study clearly indicated that CBZ increases its metabolism before 2 weeks of treatment and continues to do so till 6 weeks in Indian paediatric patients. Thus a single CBZ plasma concentration estimation in the start of the study does not serve a basis for predicting steady state concentration. Moreover, one should be aware of the possibility of autoinduction with CBZ therapy before increasing its dose or adding other antiepileptic drugs. Increase in CBZ serum concentration above maximum therapeutic concentration can lead to adverse side effects like ataxia, diplopia, vertigo, aplastic anaemia, hepatotoxicity, hyponatremia, leukopenia, GIT irritation and CBZ induced exfoliative dermatitis[11,12]. Genetic and ethnic variations in pharmacokinetics of CBZ should also be kept in mind and each patient should be monitored individually. Moreover, one should always keep patient on single drug than multiple drugs to avoid drug interactions and associated adverse drug interactions.

Table 2 : Plasma levels of CBZ in Indian Paediatric Patients of Epilepsy after 4 hours of drug dose

Weeks	Plasma Levels (Mean ± SD) in µ/ml)	P Value
0	13.93 ± 5.49	
2	12.14 ± 3.34	0.009*
3	11.85 ± 6.89	0.044*
4	10.42 ± 5.17	0.008*
6	9.95 ± 2.53	0.0005*
8	9.93 ± 2.23	0.0005*

*In comparison to values at) weeks

After application of ANOVA P Value < 0.0001, F ratio 9.829, df = 5,78.

Intergroup comparison between 2 and 3 weeks P= 0.778, between 3 and 4 weeks P = 0.201, between 4 and 6 weeks P = 0.230, between 6 and 8 weeks P >0.05, between 2 and 4 weeks P = 0.32, between 2 and 6 weeks P = 0.0002, between 2 and 8 weeks P = 0.0002, between 3 and 6 weeks P = 0.047, between 3 and 8 weeks P = 0.011, between 4 and 8 weeks P = 0.0004.

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Basics Of Convulsive Disorders:- Febrile Seizures

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Febrile seizure is the most common disorder faced in pediatric neurology. Two third of children with history of seizure have febrile seizure[1]. Lenox in 1949 wrote that febrile seizures may cause brain pathology with transient or permanent neurological deficit. In contrast Robinson in 1991 referred febrile seizures as having a "generally excellent prognosis"[2]. To make the diagnosis of febrile seizures, there must be documented fever and a clear cut history of convulsions. It is important to note that syncope in small in small childen may be precipitated by fever[3]. Therefore one must exam and investigate a child with fever carefully especially if it is the first febrile seizure.

A. Strong history of febrile seizures in siblings and parents suggest that it has a genetic predisposition. During past two decades the debate on febrile seizures has shifted from their natural history to their treatment.

DEFINITION;

The National Institute of Health (NIH) consensus conference, has defined febrile convulsion as " an event that occurs between the age of 3 months to 3 years and that is associated with fever without evidence of intracranial infection or other defined neurological cause and without a history of previous febrile seizures." NIH has not given the precise temperature at which a seizure is considered febrile cohort studies have shown that febrile seizures is usually associated with a core temperature that rapidly increases to 39oC or greater[5]. The commission on Epidemiology and prognosis of the International League Against Epilepsy has defined a febrile convulsion as "an epileptic seizure occurring in childhood after age one month, associated with a febrile illness, not caused by an infection of the CNS, without previous neonatal seizures or previous unprovoked seizure and not meeting the criteria for another acute symptomatic seizures"[6]

National collaborative perinatal project (NCCP) has sub-classified febrile seizures into Simple febrile seizures and Complex febrile seizures. Complex febrile seizure is one:-

a) which lasts for more than 15 minutes.
b) Which recurres within 24 hours.
c) Which has focal features.
d) Which has abnormal neurological satus.
e) With history of febrile seizures in parents or sibling.

Simple febrile seizure is one which does not have complex features.

INCIDENCE AND PREVALENCE

Between 2 and 4% of all children have one or more febrile seizures by the age of 5 years. In America Nelson and Ellenberg reported an incidence of 3.5% in white and 4.2% in black children. In Japan the rate is reported to be 9-10%. This may be due to genetic susceptibility. Seizure is usually associated with a core temperature that rapidly increases to 39oC or greater[5].

National collaborative perinatal project (NCCP) has sub-classified febrile seizures into simple febrile seizures and complex febrile seizures. Overall prevalence is about 4-5% . A higher incidence is noted in boys as compared to girls in the ratio ranging from 1.1:1 to 4:1. 80% seizures are generalized and simple. A febrile seizure can be partial or generalized type. 4% of children have focal onset and 0.5% have focal deficit (Todds' plasy). Tonic, clonic even atonic episodes may characterize febrile seizures[1]. 18% children have complex seizures in America, 22% in Britain and 8.6% in Scandinavia. In an effort to predict which child is at a risk of febrile seizures, four risk factors have been identified:-

1) Febrile seizures in first or second degree relative.
2) Neonatal discharge at 28 days or later.
3) Parental report of developmental delay.
4) Day care attendance.

With two of these risk factors, the probability of a child developing febrile seizures is approximately 30%1.

AETIOLOGY

A strong family history in parents or siblings suggests a genetic background. Family studies have shown that simple febrile seizures may be inherited as an antosomal dominant trait with high penetrance. Gene of febrile seizures has been mapped to chromosome 19 P and 18 Q 13-21. Other studies have shown that epilepsy with febrile seizures is an important childhood genetic epilepsy syndrome with heterogenous phenotypes[10].

PRECIPITATING FACTORS.

The height and duration of fever is important in evaluating febrile seizures but recording the temperature is not usually possible because these seizures usually occur randomly at home.

Viral infections commonly cause the fever leading to febrile seizures. Synthesis of immunoglobulin in CSF of children with febrile seizures has been demonstrated, suggesting that encephalitis may sometimes occur and not recognized[11]. There is an evidence that exenthem subtium is frequently accompanied with febrile seizures. Acute HIV -6 infection is a cause of febrile seizures[12]. Bacterial infections like urinary tract infections, shigella, otitis media and pneumococcal infections are associated with febrile seizures. Recent study has shown increased risk of febrile seizures on the day of receipt of DPT vaccine and 8-14 days after MMR vaccine, apparently not associated with long term adverse consequences[13].

OUTCOME

Approximately 30-50% of children have recurrent seizures of these half will have three and 9% will have more than three. Most important risk factor for recurrence is the age of onset. 50% of children younger than 1 year experience recurrence as compared to 28% of children who develop first febrile seizure after 1 year of age[1]. Focal, prolonged or complex events increase risk so far as recurrence is concerned. Risk factors which predict recurrence include:-

a) a history of febrile seizures in first degree relative.
b) A seizure induced by low grade fever.
c) A brief duration between the onset of fever and the convulsion.

Although the children with simple febrile seizures are at no greater risk of later epilepsy than the general population, some factors are associated with increased risk. These include:

a) Presence of atypical features.
b) Abnormal post ictal period.
c) Positive family history of epilepsy
d) Febrile seizures before 9 months of age.
e) Delayed developmental mile stones.
f) Pre-existing neurological disorder[5].

The chances of developing epilepsy is 90% when several risk factors are present as compared to incidence of 1% in children who have febrile seizures and no risk factors.

The consequences of febrile seizures on developmental milestones and behavior appear to be limited. No residual neurodeficit occurs even in children who had convulsions lasting over 30 minutes. Studies have shown no difference between controls and children with febrile seizures in IQ testing and academic performance. Immediate short term change in behavior has been reported in upto 35% children after febrile convulsions but long term follow up shows no difference in behavior in these two groups. The relation ship between febrile seizures and temporal lobe epilepsy (TLE) is recognized. Controversy exists as to whether hippocampal sclerosis of TLC is a pre existing cause or a consequence of

febrile seizure. Better neuro imaging techniques have shown that mesial temporal lesion of TLE existed before the onset of febrile seizures, so the role of febrile seizures as a cause of TLE remains controversial. Two synoumes have been recognized to be associated with recurrent febrile convulsions.

a) Hemiconvulsion, hemiplegia, epilepsy (HHE)
b) Progressive myoclonic epilepsy (PME) of childhood.

In HHE a normally developing child develops febrile status epilepticus characterized by hemiconvulsion and a persistant post ictal deficit. HHE begins abruptly and triggering cause is not known. In some patients coagulation defects with infection is believed to be the cause. In progressive myoclonic epilepsy of childhood, the child presents with recurrent febrile seizures in first year of life. These seizures are often lateralized. During ensuring months progressive decline in congnitive skills occur.

There is no evidence that febrile seizures are associated with increased mortality[14].

MANAGEMENT

First objective is to control the convulsions, then the temperature should be measured to confirm that the child is febrile. It is important to determine whether or not the fever preceded the convulsion. The history and the examination will provide the clue about the cause of fever.

ADMISSION TO HOSPITAL:

Febrile convulsion usually stops with immediate intervention. If it does not the childe should be admitted to hospital following factors favour admission after first convulsion.

a) Complex convulsion
b) Child aged less than 18 months
c) Review by doctor at home not possible.
d) Unusual parental anxiety.

INVESTIGATIONS:

Investigations usually are not needed in febrile seizures:- Investigations are needed to find out cause of fever.

LUMBAR PUNCTURE:

The most important aspect of diagnosis is to rule out an underlying infection of the central nervous system. Clinical signs will clear the diagnosis of meningitis and encephalitis in most of the cases. However in children less than 18 months of age, these signs can be subtle or absent. The decision to perform lumbar puncture in such cases is critical one. Recommendations to do lumber puncture in first febrile convulsions are:

-If there are signs of meningismus
-If the convulsions are complex.
-If child is unduly drowsy, irritable or systemically ill.
-If the child is less than 18 months old (Probably) and almost certainly if the child is aged less than 12 months.

Doctor should reassess the child again after few hours to assess the decision of not performing lumbar puncture is correct. One should never assume that a child with previous febrile seizure will not develop meningitis and one should always observe children with persistent fever even if the initial lumbar puncture is negative. Children with initial normal Lumbar puncture may later develop bacterial meningitis[14].

ELECTROENCEPHALOGRAM(EEG):

The value of the EEG in evaluation of febrile seizures has been disappointing. It is abnormal early on in 2/3rd of affected children. Both focal and generalized abnormalities have been described in immediate port ictal period but these abnormalities are not predictive of either the risk of a recurrence or the risk of long term epilepsy[1].

Reported abnormalities of EEG include:

1) Focal slowing mainly over occipital regions (5%).
2) Focal sharp waves, mainly temporo occipital region (3%).
3) focal or multifocal spikes (1.6%).
4) Hypnologic bursts.
5) Generalized spike discharge.

EEG is recommended only to rule out encephalitic process in a child with complex febrile seizures or abnormal post ictal course. No routine EEG is recommended for simple febrile seizures[1].

TREATMENT OF THE ACUTE ATTACK:

Most of the febrile seizures stop till the patient is brought to hospital. In rare instances the child continues to have a seizure upon arrival at the hospital or has a prolonged recurrence in hospital. In such cases actual treatment may be initiated. Diazepam 0.5 mg to 1 mg per kg is given parent rally. Rectal diazepam .5 mg/kg and rectal Lorazepam 0.1 mg/kg also stops an attack. Fever should be controlled by acetaminophen 1.5 mg/kg/dose to be given every 4-6 hours when rectal temperature exceeds 37.9oC. If the child is vomiting acetaminophen can be given rectally. If fever does not come down ibuprofen 5 mg/kg/dose with acetamophen 10 mg/kg/dose can be given. This combination reduces fever there is significant seizure reduction. Studies have shown that acetaminophen is more effective in controlling fever than the physical methods such as fanning, cold bathing and tepid sponging[13].

PROPHYLACTIC TREATMENT:

a) Intermittent prophylaxis
b) Continuous prophylaxis

INTERMITTENT PROPHYLAXIS:

Intermittent prophylactic oral or rectal diazepam reduces the number of recurrences in febrile seizures. Diazepam prevents seizures when given at the onset of fever. Phenobarbitone is needed in large dose and its effective blood concentration reaches in 90 minutes so it is not recommended. Oral diazepam of 1 mg/Kg/day or 0.3 mg/kg/dose q 8 hourly is very effective in reducing the recurrence. It can be continued for 2-3 days. Side effects of diazepam include ataxia (30.0%) lethargy 28.8% and irritability 24.2%15.

c) CONTINUOUS PROPHYLAXIS:

Phenobarbitone at a dose of 4-5 mg/kg/day reduces the number of recurrences in febrile convulsions and causes: behavioral side effect and cognitive dysfunction and is not recommended. Sodium valproate has also shown to reduce the recurrence rate but the potential risks of drug do not justify its use in a disorder with an excellent prognosis. Despite evidence that the drugs can reduce the recurrence, there are good arguments that prophylactic medication is rarely indicated. Recent study has shown that overall continuous prophylaxis with Phenobarbitone or valproate did not lessen the risk of recurrence in febrile convulsions so these drugs are not recommended[5].

CONCLUSION:

Febrile seizures are common and benign disorder. Majority of the children have one attack in lifetime and subsequently have normal intellectual behavior and neurological function. In more than 80% of children febrile seizures present the expression of a genetically inherited response to fever. For these children no treatment is required and parents should be reassured. Rarely febrile seizures represent little evidence for later epilepsy. Lumbar puncture is not routinely recommended except to rule out CNS infection and in children younger than 18 months. EEG is not predictive of later epilepsy in children with febrile seizures. Diazepam given intermittently in patients of febrile seizures reduces the chances of recurrence. Rarely should daily prophylactic anti convulsant therapy be considered for use in children with febrile convulsions.

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ABSTRACT ABSTRACT ABSTRACT

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TABLE 1 : RISK FACTORS FOR DRUG ABUSE

Risk factor	Substance use (%)N=58	Odds ratio (95% CL)	p.value
Nuclear family	24(42)	2.6(1.1,6.7)	0.03
Death of father	6(11)	-	0.59
Death of mother	7(12.5)	-	0.85
Presence of step-parents	6(10.7)	-	0.10
Domestic violence	23(41)	2.46(1.04,5.87)	0.04
Maltreatment at home	19(34)	4.5(1.9,10.7)	0.0002
Substance use in family	25(42.5)	-	0.13
Unemployment	13(24%)	3.7(08,19.4)	0.04

It reflects the access to a large variety of narcotic drugs, ineffective implementation of existing legislations and lack of proper drug act in Kashmir.

Maltreatment at home, domestic violence, unemployment and easy access to narcotic drug creates an atmosphere conducive for indulging in drug abuse. Maltreatment at times emerged as the only significant predictor of drug abuse in present study. The results are similar to other studies[6-8].

The knowledge of harmful effects did not deter the subjects from indulging in drug abuse. This factor needs strong consideration while devising preventive interventions against drug abuse.

It was found that drug abuse in the family did not increase the risk of drug abuse in subjects. This finding was different from other studies[9].

The present study has some limitations. The results are based on the information given by subjects, who may have under reported because of social stigma attached to consumption of intoxicating substances. Also information regarding the frequency, regularity and duration of consumption was not available to allow identification of physical or psychological drug dependence.

CONCLUSIONS

The number of youngsters indulging in drug abuse is increasing. It is related to their maltreatment at home. Early diagnosis, treatment and rehabilitation are important steps in management. Strict legislation should be made to prevent drug abuse.

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Prevalence of Goitre in school children aged 6-12 years in district Budgam (Kashmir division)

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ABSTRACT

The study was done in Budgam district, wherein 3200 children were surveyed using 30 cluster sampling technique. Overall prevalence of grade 1st goitre was found in 5.40% (5.85% in girls and 5.03% in boys). Grade 2nd goitre was noticed in 0.17% of surveyed children (0.96% in Girls & 0.48% in Boys). Total goitre rate (TGR) which is the sum of grade '1st & Grade 2nd was found in 5.57% of children. In Girls the rate was higher to an extent of 6.8% as compared to Boys were it was 5.51%. We found that grade 1st goitre was more common in the age group of 12 years were it was to the extent of 9.75% followed by age group of 11 years were it was 7.57%. Maximum TGR (total goitre rate) was found in the age group of 12 years. In boys the maximum involvement was seen in age group of 12 years (9.82%) followed by that of 7 years (7.27%). In girls maximum involvement was found in age group of 12 year's (10.57%) followed by that of 11 years (6.69%).

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Introduction:

Goitre is the name given to an enlargement of thyroid gland. One of the most important and well known global nutritional problems is iodine deficiency (ID). An estimated population of 1000 million are at risk because they live in an environment where the soil has been depleted of iodine [1]. Worldwide, over 600 million people have goitre and 20 million have some degree of brain damage (6 million are cretins) caused by the effects of iodine deficiency in pregnancy [2]. According to the World Health Organization (WHO), a total goitre rate of 5% or more in primary-school children (6-12 years) should signal the presence of a public health problem [3].

The most important single cause of iodine deficiency is inadequate iodine intake. Goitre is prevalent worldwide and in India it is also widely prevalent with different states giving rates of prevalence. As such no study estimating IDD prevalence at all India level is available on children although a few region wise studies are available. As per ICMR report on Micronutrient Profile in India (2004) the prevalence of goitre in 6-<12 years is 9.98%. These figures are from the ICMR project running from 1997 to 1999 [4] In J&K the figures also vary from one place to another. The district wise data available for J&K shows that 14 districts out of 15 districts are endemic for IDD. The prevalence in Srinagar district was to the extent of 4.46% in the same age group . A study by Zargar et al [5] in 1996 in Budgam area in the age group of 5-15 years old found the prevalence to be 44% in males & 33.8% in females in school going children . The previous year study (2003-2004) by our department in the Srinagar district in the age group of 6-12 years found that total goitre rate was to an extent of 15.27% (17% in girls & 13.67% in boys) [6] Because of the widely prevalent situation in the state the present study was contemplated.

Methodology:

The study was conducted in district Budgam from October 2004 to mid December 2004. 3200 subjects were screened. The subjects were aged 6-12 years. Two-stage cluster sampling was used to select the study sample. In the first stage a total of 30 clusters (Schools) was selected based on probability proportionate to the size of the target population in different zones. Thirty clusters were selected to ensure a valid estimate of the prevalence of the problem. In the 2nd stage 160 children within each cluster were selected. Adjacent school to the study one was surveyed if the number of children selected were not got from cluster. Since no male female discrimination of schools occurs at this level so the schools were studied as such. The number of children per cluster was based on the estimated prevalence of 20% with 95% confidence interval with a relative margin of error 10% & a design factor of 2. The formula used to calculate the sample size used was:

$$N = \frac{(Z\alpha)2\ Q}{(L)2\ \ P}$$

Where P= expected prevalence

$Z\alpha$ = standard normal deviate (corresponding to α level of significance)

L= relative margin of error

Q= I-P

FINAL SAMPLE SIZE = design effect x N

No of clusters = 30

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Sample size per cluster: total sample size
30

Data were collected using a specially designed questionnaire, including information about name, zone, school, exact age of the child and sex. Clinical examination of the thyroid gland of each child was done through inspection and palpation. Classification of goitre grading was based on the criteria endorsed by WHO/United Nations Children Fund/International council for the control of iodine deficiency disorders, which is as follows:

0 = No palpable or visible goitre

1 = A mass in the neck that is consistent with an enlarged thyroid that is palpable or visible with neck in extended position but not in neutral position. It also moves up in the neck on swallowing

2 = A swelling in the neck that is visible in a neutral position and is consistent with an enlarged thyroid when the neck is palpated

The sum of grades 1 & 2 was taken as total goitre rate.

OBSERVATIONS:

Total children surveyed were 3200 in the 30 cluster (schools) of district Budgam with 160 children in each cluster being surveyed. These accounted for about 1748 Boys & 1452 Girls. As for as overall prevalence of grade 1st goitre is concerned, we found that 5.40% of the children had grade 1st goitre with figures higher in girls to the tune of 5.85% and in boys it accounted for 5.03%. Grade 2nd goitre was noticed in 0.17% of surveyed children being to the extent of 0.96% in Girls & 0.48% in Boys. Total goitre rate (TGR) which is the sum of grade '1st & Grade 2nd was found to the extent of 5.57%. In Girls the rate was higher to an extent of 6.81% as compared to Boys were it was 5.51%. The relevant details are shown in table 1 . As regards magnitude of grade, 1st goitre in different age groups as well as sex differentiation is concerned; the details are shown in table 2. As regards total goitre rate as per sex & age group, the relevant details are shown in table 3

Table 1
Overall prevalence of Goitre:

Grade of Goitre	Total (M+F) %	Boys %	Girls %
G1	5.40	5.03	5.85
G2	0.17	0.48	0.96
TGR	5.57	5.51	6.81

Note: G1 = grade 1st goitre, G2= grade 2nd goitre,
TGR= total goitre rate (G1+G2)

Table 2
Prevalence rate of grade 1st goitre in different age groups as per sex

Age group	Overall (M+F) %	Boys%	Girls%
6	5.28	5.86	4.5
7	6.18	7.27	4.76
8	4.08	3.70	4.61
9	6.45	6.88	5.88
10	5.28	5.85	4.68
11	7.57	4.88	5.80
12	9.75	9.37	10.13

Table 3
Total Goitre Rate in different age groups as per sex

Age group	Overall (B+G) %	Boys%	Girls%
6	5.28	5.86	4.5
7	6.18	7.27	5.23
8	4.08	4.07	5.12
9	6.45	6.88	6.37
10	5.28	5.85	5.20
11	7.57	5.33	6.69
12	9.75	9.82	10.57

Discussion:

Goitre is still a big public health problem in various districts of Kashmir valley. We found that 5.40% of the children had grade 1st goitre with figures higher in girls to the tune of 5.85% and in boys it accounted for 5.03%. Grade 2nd goitre was noticed in 0.17% of surveyed children being to the extent of 0.96% in Girls & 0.48% in Boys. Total goitre rate (TGR) which is the sum of grade '1st & Grade 2nd was found to the extent of 5.57%. In Girls the rate was higher to an extent of 6.81% as compared to Boys were it was 5.51%. Zargar AH et al (1997) found the TGR to be 52.08% with G1 in 41.95% & G2 of 10.1% in Baramulla district of Kashmir valley. The prevalence was more in males to the extent of 52.08% & in girls it was 49.23%[7] In 1995 in there study in school children aged 5-15 years in Kashmir valley found a TGR of 45.2%. 43.9 % in boys & 46.23 in girls.37.74% of children had grade 1st goitre while as 7.44% had grade 2nd goitre [8]. Their study in 1996(a) found the rate to be 44% in males in age group of 5-15 & 33.8% in females in Budgam area [5]. Our figures are lower possibly because of better awareness & sustained IEC activities by the Government about the use of iodized salt and possibly because the age group included was lower. Kapil U et al (2003) in there study in school children aged 6-12 years which they did in Bharatpur district of Rajesthan found the rate to be 7.2% . Grade 1st goitre was seen in 7% & grade 2nd goitre in 0.2% of children. As for as sex is concerned the rates of G1 goitre was 5.7% & 7.9% in girls & boys respectively [9]. Chandra AK et al (2001) in their study in children aged 6-15 years found the TGR to be 21.6% with G1 in 20.2% & G2 to be 1.4% [10]. Brahmbhatt S (2000) in their study in Dang & Baroda districts of Gujarat found the TGR to be 29.6% with G1 in 29.2% & G2 in 0.4 %.[11] Our figures correlate well with there findings. Our figures also correlate with that of Bhardwaj AK et al (1997) who found the TGR to be 20.5% with G1 in 17.8 & G2 in 2.7% of children aged 6-12 years. The rate was found to be 39.3% in boys and 18% in girls. [12]

Grade 1st goitre was more common in the age group of 12 years were it was to the extent of 9.75% followed by age group of 11 years were it was 7.57%. Concerning the sex differentiation it is evident from the table that the prevalence was more in age group of 12 years in boys (9.37%) followed by age group of 7 years were it was 7.27%. In girls, the magnitude was found to be higher in the age group of 12 years were it was found to be 10.13% followed by age group of 11 years were it was 5.88%. In the study by Chandra et al in tripura the maximum involvement was seen in age group of 11 years to the extent of 24.1%.

CONCLUSION & ECOMMENDATIONS

Goitre is still a major public health problem in J&K. although drastic decrease in the magnitude of the problem has occurred in few years. In this connection we would like to suggest the following measures.

- A Goitre cell needs to be established & strengthening of the same with expertise from community medicine department.
- Current iodine deficiency is depicted by urinary iodine levels. In this connection proper lab facilities for urinary iodine excretion as well as for checking the iodine content of salt need to be set up.
- It is also essential to set up one district level IDD

monitoring laboratory for iodine content of salt and Urinary Iodine Excretion for monitoring proper implementation of the IDD Control Programme.

- The iodized salt should be distributed through public distribution system also.
- Sustained IEC (Information, Education and Communication) involvement should be ensured so that people are made aware about the consumption of iodized salt. Help of field publicity wing of the Information Department of J&K & Health Education Bureau also needs to be taken. To intensify the IEC activities a communication package by way of video films, posters/danglers and radio/TV spots need to be finalized

The goitre prevalence rate although very high in district Budgam yet it appears that the magnitude is lower as compared to other districts as per hospital OPD attendance. Thus to find the exact magnitude of the problem in whole Kashmir valley the survey needs to be done in other districts also.

To prevent loss of iodization because of environmental loss what is needed is production facility in state also so that this problem is checked. Quality control of the salt with repeated lab investigations thus is very much needed.

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Anatomical variation of superficial branch of radial nerve - A Cadaveric Study

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ABSTRACT

The course of superficial branch of radial nerve (SBRN) has not been studied well. The available literature on SBRN is on western population only. The aim of this study is to delineate the normal course & variations in Indian population and to manifest surgical implication of this study. Thirty cadaver extremities were dissected and the course of the SBRN was delineated. Bony landmarks were identified, marked with pins and the relationship of the nerve and its branches with the bony landmarks was studied. The distance between the bony landmarks and the points at which nerve originated, became superficial and branched was measured. A common pattern of the course of the SBRN was seen in only 18 (60%) specimens. In these specimens the origin of the SBRN was below the lateral humeral epicondyle, the nerve became superficial by piercing the forearm fascia and the nerve progressed distally as a single trunk and was placed radial to the Lister's tubercle. At the level of radial styloid or immediately after leaving the radial styloid the nerve divided into 3 to 5 branches and was placed over the first dorsal compartment. In remaining 12 (40%) specimens a number of variations were observed. The origin of the nerve was at the level of lateral epicondyle in 3 specimens and above the epicondyle in 7 specimens. In one specimen a motor branch emerged during its deep course. In three specimen's nerve branched in its superficial course. The nerve is at a great risk during various surgical procedures. Inadvertent injury to the SBRN can cause debilitating postoperative neuritis. The course of the SBRN showed significant variations in the group and only 18 (60%) specimens had a common pattern in its course. A number of differences in the course of the SBRN in our population and those in the Western population were observed.

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Introduction

Since the 19th century, the distribution of the radial sensory or superficial branch of the radial nerve (SBRN) has been documented in the anatomic texts and surgical atlases. The described course of the nerve, however, varies in textbooks and only few studies that accurately depict its course have been conducted[1,2]. These studies have reported great variability in patterns of course branching and as well as anomalies of distribution. Since the nerve is purely sensory, it's taken for granted that its injury does not affect motor function and due to its anatomic location its injury is not considered to hamper daily activity. However, once it gets injured it not only results in excruciating pain and insensitive skin over dorsum of first web space but also results in painful neuroma and discomfort feeling in hand persisting for a long time[3,4].

There have been few anatomic studies of SBRN during past 80 years. In 1985, Mackinnon and Dellon[4] outlined pattern of this nerve. Leao[5], in 1958, noted the number of branches at the radial region of the wrist. Specific measurements and pattern of branching was noted by Auerbach[2] and Abrams[1] in 1994 & 1992 respectively. In 2003 Sawaizumi[6] reported injury to SBRN on the wrist joint, caused by intravenous injection of a needle. These studies have been done in the Western population and may not represent the course of the nerve in other population groups.

The aim of this study was to identify the anatomical variations in the course of superficial branch of radial nerve, to highlight the differences in its course between our study and what is available in the literature and to provide guidelines so that the risk of injury to this nerve is reduced.

Materials and Methods

Thirty cadaver extremities with no known history of disease or trauma to the limbs were dissected. Lateral humeral epicondyle, radio-capital joint, radial styloid and the first dorsal wrist compartment were selected as landmarks and marked with reference pins. The length of forearm was measured from lateral humeral epicondyle to the radial styloid. The radial nerve was identified in the interval between the brachioradialis and brachialis and was dissected in a proximal-to-distal direction. The bifurcation between the deep and superficial branches of the radial nerve (origin of SBRN) was identified, and its relationship to the lateral humeral epicondyle identified. The distances between point of origin of SBRN to lateral humeral epicondyle and radio-capital joint were measured. Next we measured the distances from the radial styloid to the points where nerve first became visible from under the brachioradialis and where it gave its first branch. We carefully observed the number of branches of SBRN crossing the wrist joint and width of zone of these branches was measured. We also observed the relationship of branches to the first dorsal digital compartment.

All measurements were determined by means of a divider ID N0107108 (Camlin Limited Mumbai India, accurate to 0.1 mm). Sketches were drawn and photographs were taken for each dissection. Normality of measurement was confirmed and means and standard deviations were determined by means of the SPSS

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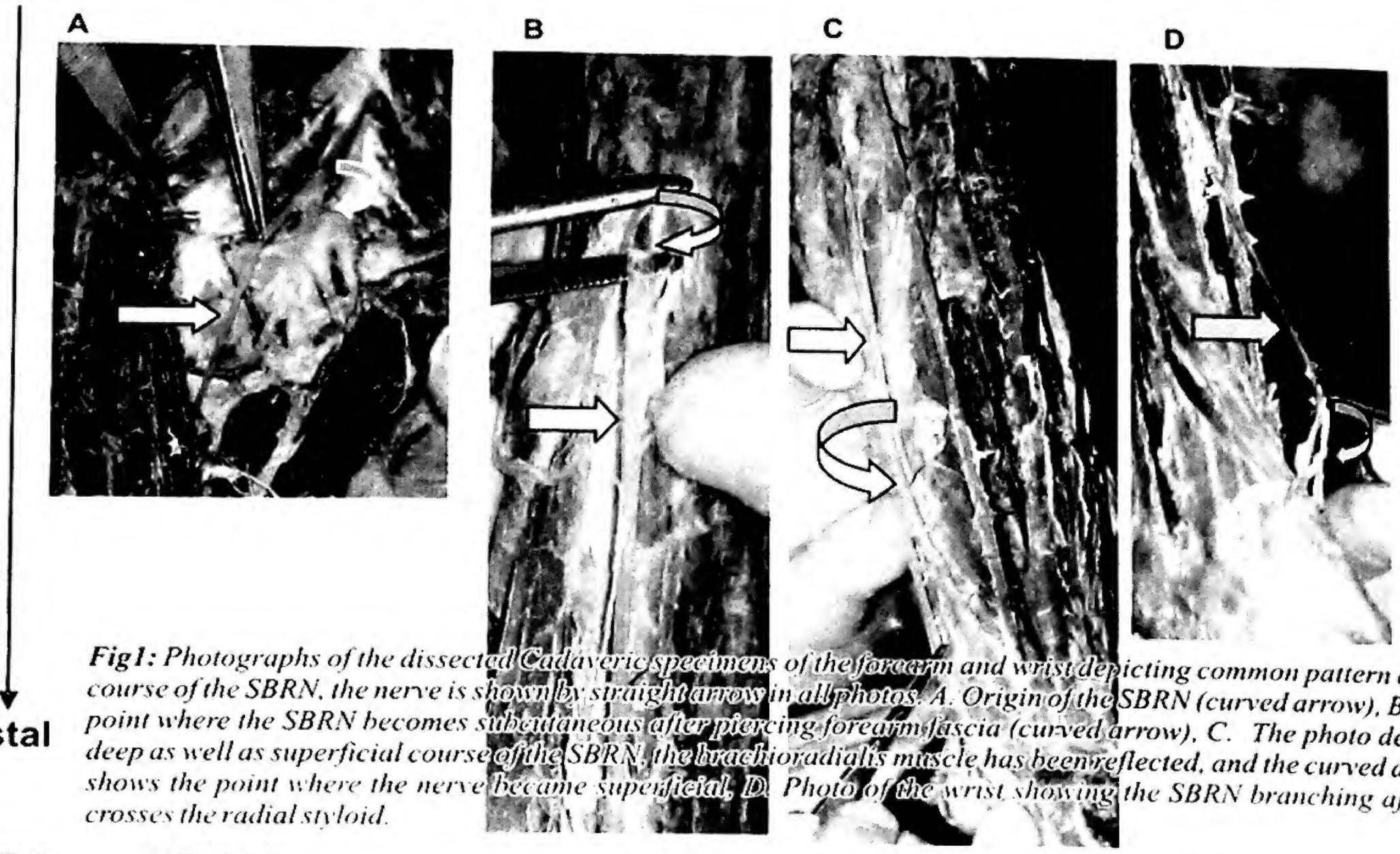

Fig1: Photographs of the dissected Cadaveric specimens of the forearm and wrist depicting common pattern of the course of the SBRN, the nerve is shown by straight arrow in all photos. A. Origin of the SBRN (curved arrow), B. The point where the SBRN becomes subcutaneous after piercing forearm fascia (curved arrow), C. The photo depicts deep as well as superficial course of the SBRN, the brachioradialis muscle has been reflected, and the curved arrow shows the point where the nerve became superficial, D. Photo of the wrist showing the SBRN branching after it crosses the radial styloid.

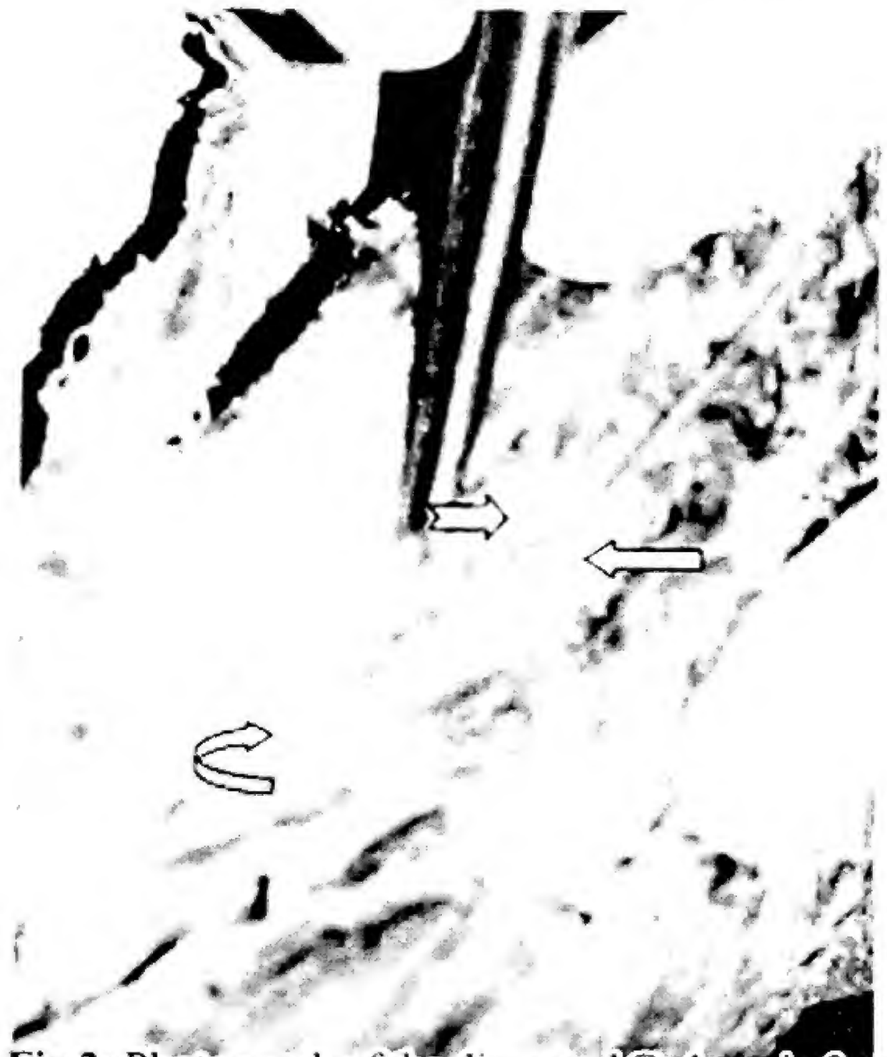

Fig 2: Photograph of the dissected Cadaveric forearm showing motor branch of the SBRN to Extensor Carpi Radialis Brevis. The point of origin of the SBRN is shown by curved arrow. The SBRN is shown by straight arrow. The motor branch of the SBRN is shown by arrowhead.

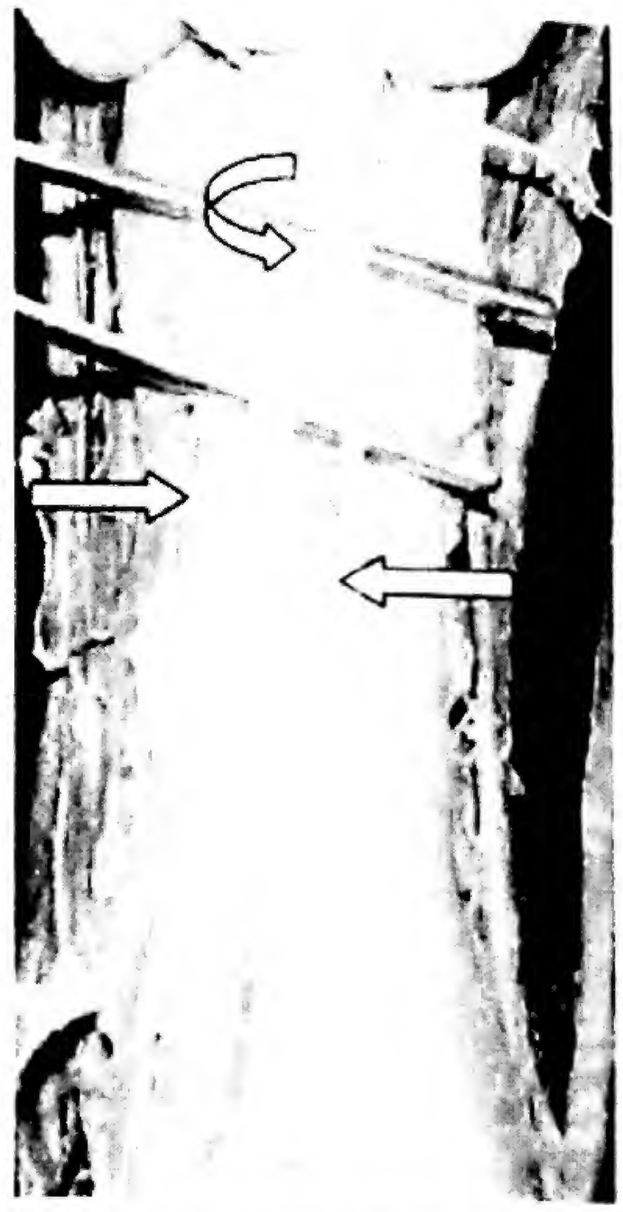

Fig 3: Photograph of the dissected forearm depicting the branching of the SBRN immediately after it became superficial. The point where nerve became superficial is shown by curved arrow and the 2 branches are shown by straight arrows.

software program (SPSS for Windows, Standard Version Copyright © SPSS Inc, 1989-1999).

Results

The most common pattern of the SBRN, which was seen in 16 specimens (53.3%), is shown in Fig 1 (A to D). The SBRN arose from the radial nerve at the level of the lateral epicondyle in 2 specimens (6.6%), above the lateral epicondyle in 12 specimens (40%) and below the lateral epicondyle in 16 specimens (53.3%). The distances from the point of origin of SBRN to lateral epicondyle and radio-capital joint were 2.09cm (range 0.6 to 4.9cm, S.D 1.162) and 1.91cm (range 0 to 5.9cm, S.D 1.593) respectively. The SBRN was radial to radio-capital joint in 27 specimens and crossed over the radio-capital joint in 3 specimens. The SBRN coursed distally deep to brachioradialis muscle and emerged between the tendon of brachioradialis and the extensor carpi longus and pierced the forearm fascia in all specimens. In one specimen the SBRN 3 cm from its origin gave a motor twig to extensor carpi radialis brevis, is shown in Fig 2.

The SBRN became subcutaneous 7.92cm (range 2.9 to 11.0cm, S.D 2.270) proximal to the radial styloid. The point at which the SBRN became subcutaneous was, on average, the distal 29.85% (range 10.9 to 42.5%) of forearm (the distance from the lateral humeral epicondyle to the radial styloid). The SBRN progressed distally as a single trunk in 27 specimens and was placed between radial styloid and Lister's tubercle in 11 specimens (36.6%), over the radial styloid in 17 specimens (53.3%) and

Table 1: The relationship of the superficial branch of radial nerve (SBRN) with respect to bony landmarks in 30 Cadaveric specimens studied.

	FR (cm)	LE-N (cm)	RC-N (cm)	RS-N (cm)	RS-N/FR (%)	RS-LS (cm)	LS-N (cm)	NB (number)	WB (cm)
mean	26.7	2	1.9	7.9	29.8	2.3	1.9	3.1	2.7
SD	1.5	1.1	1.5	2.2	8.5	0.3	0.6	1.3	0.8
minimum	23.5	0.6	0.0	2.9	10.90	1.8	0.3	1	1.5
maximum	31	4.9	5.9	11	42.50	3	3	5	4.1

FR: length of forearm. **LE-N**: distance from lateral epicondyle to origin of SBRN. **RC-N**: distance from radiocapital joint to origin of SBRN. **RS-N**: distance from radial styloid to where SBRN became superficial. **RS-N/FR (%)**: the percent distal forearm length onwards from the point where SBRN became superficial. **RS-LS**: distance from radial styloid to Lister's tubercle. **LS-N**: distance from the Lister's tubercle to main nerve trunk or its nearest branch. **NB**: number of branches of SBRN at wrist.
WB: width of the zone of the branches

medial to radial styloid in 2 specimens (6.6%) on the volar aspect. In one specimen the nerve trunk branched immediately after it became subcutaneous, is shown Fig.3. The point at which it branched was 6.5 cm from the radial styloid. In two more specimens the nerve branched in its superficial course. These branches left the SBRN 2 cm and 3 cm from the radial styloid respectively. The radial styloid to Lister's tubercle distance was 2.31 cm (range 1.8 to 3.0cm, S.D 0.31). The main trunk of SBRN or its branches were placed radial to Lister's tubercle in all specimens and the distance between Lister's tubercle to nerve or its nearest branch was 1.96 cm (range 0.3 to 3.0cm, S.D 0.60). In 17 specimens (53.3%) nerve was found to lie directly over the radial styloid an in rest it was at a mean distance of 0.9 cms except for 2 specimens (6.6%) where it was found to be on the volar aspect of radius, 0.8 cm & 0.5 cm respectively. At the level of radial styloid or immediately after leaving the radial styloid the nerve divided at an average 3.16 branches (range 1 to 5), 2 branches in 9 specimens, 3 branches in 6 specimens, 4 branches in 6 specimens and 5 branches in 9 specimens.

Discussion

Many surgical procedures are performed over the radial dorsum of the forearm and wrist. De Quervain's disease, wrist ganglia or synovitis, extensor tendon rupture or laceration, carpel fracture, instability, arthritis and distal radius fractures are just a few of the disorders and injuries that necessitate incisions over this area. External fixator application for radius and wrist problems requires incision for pin placement in the dorsoradial side of forearm and wrist. Recently, wrist arthroscopy has gained popularity and is being used as a diagnostic and a therapeutic modality in treatment of many wrist disorders. This procedure uses portals over the dorsum of the wrist[17]

The injury to SBRN from surgical incisions has been well documented in the literature[9,11] Most of these were reported after surgical release of the first extensor compartment in De Quervain's disease. Nearly 100 years ago, Fritz De Quervain stated that "Care must be taken not to damage the sensitive branches of the radial nerve which runs run across this area towards the dorsum"[10]. Despite these documentations, damage to this nerve still occurs. Paresthesia, hypesthesia, and painful neuromas result from excessive retraction or accidental partial or complete transaction of the nerve.

In the present study we delineated the course of the SBRN with respect to easily identified bony landmarks. There are only two published recent studies which have defined the course of SBRN[1,2] Both these studies were done in Western population. The Comparison of our study with the available literature highlighted a number of variations.

The radial sensory nerve branched (at the level of lateral humeral condyle) from radial nerve above, at or below the lateral humeral condyle – 40%, 6.6% and 53.3% respectively. Abrams[1] reported all the branches were given below the lateral humeral condyle. In one specimen (3.3%) immediately after the origin of SBRN, it gave a motor twig to extensor carpi radialis brevis was observed by us. This incidence is much reported higher in the study done by Mekhail AO [18] and Salisbury[11] 13.3% and 56% respectively. As the nerve progressed it coursed deep to brachioradialis muscle and emerged between the tendon of brachioradialis and the extensor carpi longus and pierced the forearm fascia to lie superficial in the radial dorsum of the forearm. This was in all 30 specimens in this study. Appleton[19] and Linell[20] each reported a case of absence of the superficial radial nerve. Linell also reported 1 specimen where the SBRN after dividing from the radial nerve, traveled superficially to the brachioradialis along its entire course. SBRN after becoming superficial, continued as a single trunk till it reached wrist joint, except in for 3 specimens, where it branched proximal to wrist joint. Abrams[1] and Auerbach[2] have reported the nerve divides soon after it became subcutaneous into 3 to 10 branches which cross the wrist in all their specimens. The mean distance from the point were SBRN became subcutaneous to the radial styloid was 7.92 cms and on an average the distal 29.85% of the forearm. Abrams[1] reported a mean distance of 9 cms and on an average 36% of distal forearm while Auerbach[2] noted a mean distance of 6.03 cms which corresponded to distal ¼ of the forearm. As the SBRN coursed distally, in 17 specimens (53.3%) the nerve passed over the radial styloid, in 11 specimens (36.6%) the nerve passed between radial styloid and the lister's tubercle and in 2 specimens (6.6%) it was found to be on medial side of radial styloid on volar aspect of forearm. Auerbach[2] in his study reported all the branches of the SBRN passed between the radial styloid and the lister's tubercle. Finally the SBRN branched at the wrist (except for 3 specimens) with an average of 3.16 branches (range 1 – 5, S.D:1.39) in our specimens. The SBRN had an average of 5.8 branches (range 3 – 10) which crossed the wrist was reported by Auerbach[2].

In conclusion certain guidelines should be followed to reduce the risk of injury to SBRN.

The proximal pins in external fixator application for distal radial fractures are to be applied at a distance of 11 cm from the radial styloid i.e. proximal to lower 3rd of forearm. We also advocate a minimal exposure and careful retraction of the nerve if pins are to be applied more distally towards the wrist. During exposures of lower forearm and around radial styloid the SBRN and its branches should be identified and carefully retracted to avoid injury.

Better understanding of the surgical anatomy of the SBRN will aid in its protection during surgical procedures in its vicinity. It will also aid in localization of the nerve.

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Medicine and Myths; Challenges for Evidence Based Clinical Practice in Kashmir

Ayoub Mirza

Kashmiri culture is shrouded with myths, legends and mysteries. Even the word Kashmir is derived from a folklore that valley of Kashmir was once inhabited by demons headed by chief demon Jalodabhava. These demons used to terrorize the population till a mystic by name of Kashyaprishi threw a huge rock on top of Jalodbhava and buried him under it. Legend states this rock is present day Hari Parbat hill located in the heart of Srinagar. Kashmiris are still haunted by these demons in the form of various medical myths. These often lead to poor compliance, futility, loss of financial and human resources and in severe cases interference of medical management with occasional fatal consequences. It is ironic that most victims of these myths are patients being treated at institution of mental health located at the foothills of Hari Parbat. Exploring the basis of these myths and understanding the need for evidence based medicine might improve Kashmir's health care delivery and overall clinical outcome.

Origin of medical myths:

Medical myths are decades and in some cases centuries old and passed on from generation to generation by the word of mouth. Uncovering the basis of such myths is usually complex, however it is the myths generated by medical professionals in recent past that are the focus of this paper. Uncovering origins of such myths is relatively simpler. Among medical professionals myths are usually generated and dispelled because they make pathophysiologic sense. It might make sense to prescribe expectorant for treatment of pneumonia however clinical studies have disproved this. Among medical professionals there is a common belief that urinary tract infection in a young man requires evaluation with imaging and other studies. In reality extensive evaluation appears unnecessary for young men with bacteriuria who respond to antimicrobial therapy [1]. Another misbelieve among medical community is that bed rest is a useful adjunctive therapy. This has been disproved by a meta-analysis of 39 studies which showed that bed rest versus early mobilization for prevention and treatment of a variety of medical conditions is at best not beneficial and at worst harmful [2].

Myths can also be generated in medical community by isolated cases reported in the literature or more commonly by personal experiences of a practitioner. These anecdotes sometimes tend to shape the practices even though when put to test by clinical trials these beliefs may prove to be wrong. Perhaps the commonest reason for medical myths is that patients often have overambitious expectations from health professionals that we desperately try to fulfill. In this desperation and frustration we may provide explanations and advises that have never been proved by evidence. Furthermore physicians are overworked and instead of taking time to explain the nature of disease and reassurance they sometimes find it easier and quicker to prescribe a medicine or order a diagnostic test. Finally the evidence based practices are changing fast and what is believed to be evidence based medicine one day might prove to be a myth next day. If a medical practitioner does not stay up to date with medical literature they might be practicing myth without realizing it. Whatever might be the reason such myths often propagate fast as people believe that if an expert says so it must be correct thus a myth is generated and disseminated.

Some medical myths are universal while others differ spatially and temporally. People almost universally believe that cold and wet weather causes cold and upper respiratory tract infection but this has never been validated, what is well known though is that staying indoors will result in spread of viruses to other people thus propagation of diseases. Similarly belief that too much stress causes graying of hair has not been substantiated. In fact graying of hair is genetically programmed and cannot be changed by change in stress level. Some myths have cultural basis and are limited to certain cultures or countries. There is a widespread belief in Indian subcontinent that taking a medicine in capsulated form is *"Garam"* (side effect) than taking it in the form of a tablet or liquid form. In one study performed in Pakistan 51% of people in the study believed that antibiotics should be taken with milk [3]. Such beliefs might have detrimental effect by interfering with the absorption of some antibiotics and thus render them ineffective.

Medical myths change temporally; in 1692 nineteen men and women were hanged in Salem New England for practicing witchcraft. Though such myths have been almost eradicated in west they still survive to some extent in some parts of Kashmir. Epilepsy and ecclempsia are still believed by some to result from bad influence of demons *"Jin"* or spirits. This results in continuous suffering and pain and at times even death for such patients. Another example of a medical myth that changed with time is the use of beta-blockers in patients with congestive heart failure. Nearly 20 years ago prescribing a beta blocker for a patient with CHF would have been considered a malpractice. Now there is overwhelming evidence that beta blockers have a favorable effect on ejection fraction and the combined risk of death and hospitalization for heart failure [4, 5]. Despite this beta blockers are underutilized for these patients due to the persistence of myth among medical professionals.

However varied the myths may be spatially and temporally only way to dispel them is to teach, propagate and practice evidence based medicine. Most certified medial practitioners are not responsible for propagation of misbelieves but it is partly their responsibility to educate patients and care takers regarding them.

Challenges of Evidence Based Medicine:

If it is a challenge to teach EBM even bigger challenge is practicing it. In most cases this is not due to inability of medical professionals to keep up with the evidence but due to lack of it or worst yet poor or contradictory evidence. Underdeveloped regions of world are worst victims of poor evidence since most evidence for medicine comes from research done in western countries primarily USA. Research done in one part of world in a selected group of people may not have general application. There is difference in disease profile between different regions of world and most of the evidence that exists currently is for the diseases that are highly prevalent in western societies. There is plenty of evidence for coronary artery disease but very little for diseases like Ascariasis, Typhoid which are highly prevalent in valley. Chagas disease affects nearly 20 million people in Latin America and kills nearly 50,000 people every year yet there is lack of research for this disease as this is not totally relevant for developed countries. Secondly evidence for certain clinical practice does not necessarily mean that this holds true for Kashmiri population. Most of the clinical studies are done in USA and Europe and some of the data available form these studies may not be applicable to Kashmiri population for difference in genetic and environmental factors. Thus generalization should be cautiously applied. Perhaps the bigger challenge for practicing medicine that has been proved to be effective is the lack of resources. Increasing healthcare costs make it sometimes impractical to follow EBM and rationing becomes a priority than EBM. Although ICD implantation has been shown to reduce mortality compared to antiarrythmic drugs in secondary prevention of cardiac arrest and sustained ventricular tachycardia [6-10], its cost effectiveness as a society may not be justified. The mean estimated cost of a single-chamber ICD and lead system, as used in SCD-HeFT (Sudden Cardiac Death in Heart Failure Trial) was $17,500 (range, $13,300-$23,700), and the estimated cost of amiodarone was $3.53/day for the 200-mg dose. In a wealthy country like USA

this kind of therapy might be effective and realistic but in a society with limited funds where resources need to be rationed practices based on such an evidence might not only be unrealistic but also might not provide the value for money spend on per life saved.

EBM continues to evolve and changes temporally and spatially. What is evidence today may not be same tomorrow. As the time to review ever expanding literature seems to be shrinking it becomes extremely difficult to keep up to date with this changing evidence. Practicing evidence-based medicine is even more challenging in Kashmir as most of the population is not educated about this. It becomes extremely difficult to explain management of viral illness to a patient who does not understand what a virus is.

In order to manage disease properly it is essential that patient at least understand the fundamentals of that disease. Thus patient education is critical part of medical management. In the absence of such a knowledge many myths are generated which disperse among the population.

Teaching Evidence Based Medicine and other skills:

With the advent of electronic media particularly the internet and with ever expanding number of medical journals and books published learning the skill of critical review of medical literature has become essential. In order to practice EBM physicians should be proficient in reviewing literature and also deciding the quality of evidence. This learning process takes time and experience however in order to establish the culture of EBM this has to start early in the medical education and be made part of medical school curriculum. For physicians learning process continues throughout the career, however due to time constrains there is limited time to review literature for best evidence. It is equally true that in order to provide optimal care for patients they need to learn the skill of applied research principals. There are nearly 30,000 medical journals and more than 17,000 new medical books published each year (11) which makes it extremely difficult to stay up to date with the progresses and needs survival skills. These can only be achieved by establishing structured programs like continuous medical education activities, journal clubs, seminars and symposiums where new evidence can be critically discussed. This will give opportunity of obtaining best current evidences, filtering out the poor evidence and establishing protocols and clinical guidelines. Lastly these activities can also give opportunity to discuss the need for research for pathophysiology, clinical course and management of "orphan diseases" for which there is little clinical evidence due to their rarity in western world.

Clinical guidelines and consistency of care

Clinical practice guidelines have been defined as "systematically developed statements to assist practitioner and patient decisions about appropriate healthcare for specific clinical circumstances"[12]. WHO and other world health organizations have established the guidelines for almost every basic service however such guidelines can only be effectively followed if they are financially feasible and cost effectiveness of high tech and expensive medical technologies needs to be established. These guidelines should not only be based on the best available evidence but should also take into consideration whether such guidelines will be good value for the money available. Cost benefit analysis should be performed to make best use of the limited and finite resources. Thus not only physicians but also policy makers, and health care managers should participate in establishing such guidelines.

With easy access to the health care information on internet patient's expectations have increased. Thus they are becoming more and more demanding and litigious, this puts an added burden on physicians and other practitioners making it even more important to establish consistency in care and follow protocols and guidelines. Once such guidelines are established they should be followed strictly and physicians should be expected to practice guideline recommended evidence based therapies. Audits can be performed at regular intervals to check the compliance and effectiveness of the guidelines. All this needs significant commitment from government, physicians and administrators of the health institutions.

Public health education

Public education is the cornerstone of effective medical practice. A well informed patient follows medical advice more closely and effectively, this not only results in improvement in clinical outcome but also improves health care costs and leads to more efficient use of resources. It is the responsibility of every physician to educate and counsel the patients and families about disease, treatment and prognosis and to try to change the attitudes towards improvement and maintenance of health. Verbal advice is still the most effective form of patient education; this is a skill that needs to be taught at every level of physician education. In order to change attitude it is essential that patient education be made integral part of every patient encounter. We have to establish the culture of making it OK for patients to ask questions, taking time to answer them in lay language and resisting the temptation of using jargon of medical language. Nurses, dieticians, physical therapists etc can play essential role in patient education. Verbal advice can be supplemented with audio-visual aids and print materials in the form of handouts, booklets and pamphlets. At the community level government has established various programs and institutions to improve awareness of health related issues. Central Health Education Bureau (CHEB) is the apex institution for health education in India. Another institution for health education in the nongovernmental sector in India is Voluntary Health Association of India (VHAI) that was established in 1970. However due to variety of reason these institutions have had limited influence in Kashmir so far. Using these along with more traditional resources like, song and drama, games, exhibitions at the weekly market and yearly festivals, and pictorial aids will make a major difference in public health education. Also teaching the teachers like religious leaders, traditional healers and traditional birth attendants (dais) will be effective in disseminating health education.

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JK-Practitioner2006;13(3):173-175

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The only dynamic website for DOCTORS

AKAS Group has launched a newly built and the only dynamic website for doctors www.akasdoctor.com which caters many services including some which are launched for the first time in the medical industry. The services include that of Email 5GB of space here the specialty being that it's only for doctors and no one else can use this email id. This on itself creates a separate identity for a doctor. There is matrimony where only doctors profiles are listed out this are also for the first time that a matrimony site is launched only for doctors. There is also shopping where medical products are sold online this again is for the first time a site that is catered for medical items shopping alone. There is also doctors forum where doctors can post/review and discuss about medical issues online. There is medical quiz where doctors can enrich their knowledge and also gain points for prices that can be won. There is medical news; the best part about this news service is that doctors can view news relating to their topic of interest, region, national and international news as well in one box, with latest updates from around the globe.

There are services where doctors can get benefited in a huge way; they can list their old medical equipment for sale for free on the site. They can also list their hospital/clinic for sale on the site for free. They also can get a quotation from medical equipment manufacturing companies for a particular product and get the information online itself rather than wasting their precious time with sales people. Also akasdoctor.com has made it clear that it would launch one new service every month for the benefit of the doctors.

Recommendations for Undergraduate Pharmacology Practical Curriculum (For attention of MCI)

Jaswant Rai

Pharmacology is taught during 2- profession of MBBS course. Medical Council of India (MCI) recommends that at the end of pharmacology course medical students should develop "skills" to prescribe drugs for common ailments; recognize adverse reactions/interactions of commonly used drugs; observe experiments designed for study of effects of drugs, bioassay and interpretation of experimental data; scan information on common pharmaceutical preparations and critically evaluate drug formulations.[1] With present pharmacology practical syllabus (PPTS), the said objective cannot be achieved. That is why PPTS has become a source of criticism in the last few years.

There is a great doubt about the utility of training of dispensing pharmacy.[2] Experiments in experimental pharmacology were planned over three decades ago and no attempt has been made to assess either their relevance or usefulness.[3] It is not necessary that animal experiments be carried out by the students "first hand".[4] The entire scheme of PPT should be thoroughly overhauled - the actual performance of exercises in experimental pharmacology and pharmacy by the medical students should be deleted.[5] The existing undergraduate pharmacology practical curriculum has not been very useful to students and it is desirable that clinically relevant practicals to be incorporated in it.[6] Experimental pharmacology should be continued with refinement and reduction in number of animal experiments and there exists non-uniformity in pharmacology practical teaching and names of department.[7]

Present work is an attempt of framing guidelines for Revised Modified pharmacology practical curriculum to attract attention of MCI or to initiate a debate on this issue. Suggestions of above said workers , recommendations of a workshop on MBBS pharmacology practical scheme and review of Journals of 5 medical colleges (Seth GS Medical College, Mumbai,; JIPMER, Pondicherry; Pramukhswami Medical College, Karamsad; BJ Medical College , Ahemdabad; Government Medical College , Amritsar)have formed source of these recommendations.[1]

Recommendations

1. Pharmacy section in PP curriculum should be deleted. Principles of commonly used preparations like powder, mixture, lotion and ointment should be included in common dosage forms in General pharmacology section.
2. Experimental pharmacology should be continued with refinement and reduction in number of experiments.
3. Clinical exercises should be incorporated in PP curriculum.
4. Pharmacology as name of department should be replaced with clinical pharmacology.

Guidelines:

PP curriculum is divided into three sections:

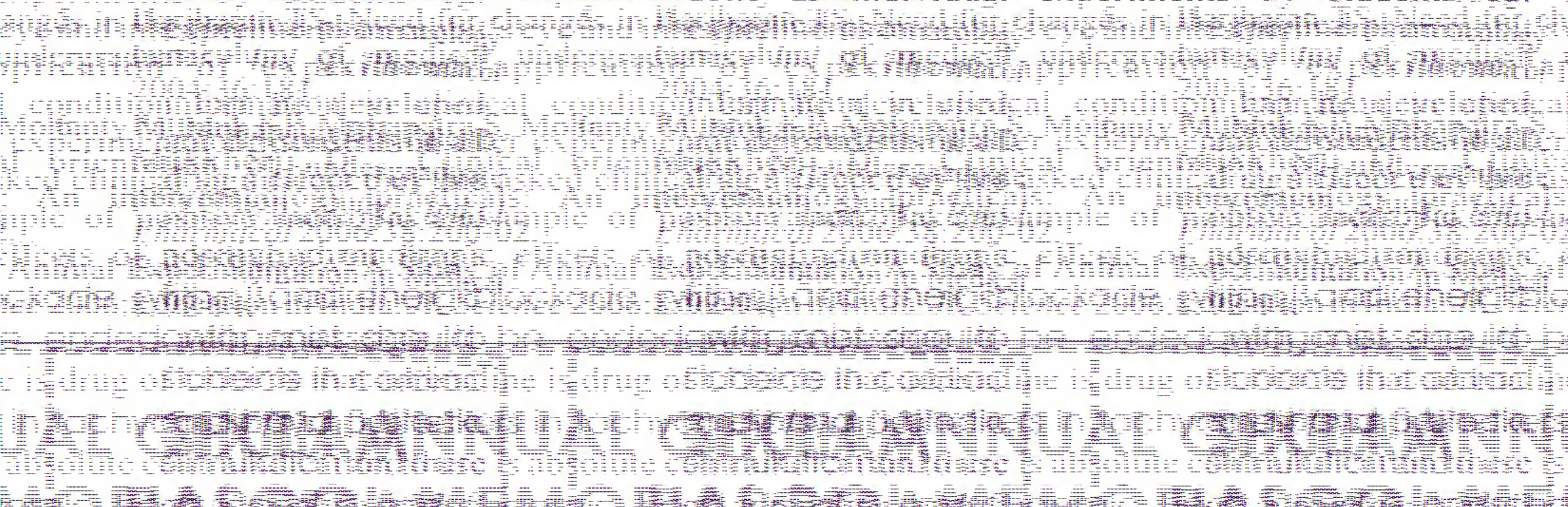
i. General Pharmacology
ii. Experimental Pharmacology
iii. Clinical Pharmacology

General Pharmacology: Outlines of exercises in this section include:

- Sources of Drugs (demonstration can be done in museum)
- Common dosage forms (demonstration of different drug dosage forms available in

comment comment comment

References



Vascular Surgeon : need of the hour

Devender Singh

While the answers to the few problems in vascular surgery are slowly emerging i.e. the refinement of diagnostic techniques and the development of biologically better small arterial substitutes, from the work of laboratory and clinical research, some problems, far removed from this scientific effort, have recently intruded into the daily life of the vascular surgeon...

WHO IS A VASCULAR SURGEON?

In a historical perspective, these problems are not unexpected. For centuries, even millennia, medicine was an undivided unitary segment of humanity's interaction with the hostility of nature. There was no conceivable reason to parcel out the meager factual cargo that encompassed the knowledge of diseases and the (usually fruitless) attempts to deal with them. A physician was a person whose identity was sharply defined within an unchanging circle of activity. It was only in relatively recent times (some 300 years ago) that the first dichotomy appeared in this image: the recognition of a new type of physician who used his or her hands in treating disease, that is, the surgeon. A veritable deluge of change came as medicine assumed the aspects of science no more than 100 years ago. Internal medicine and surgery assumed sharply distinguished silhouettes; during the last 50 years, their further fragmentation has resembled a chain reaction.

This process has forced each subdivision of the large entity of medicine to face the same problem of defining its identity, as we now see in vascular surgery. Elemental and vitally important questions arose: Is the existence of the new subdivision justified by the goal it seeks to achieve? What exactly is the scope of its legitimate interest? Who is entitled to enter it? How does one acquire this entitlement?

The difficulties do not lie only at the clinical level; a mundane concern also enters the picture. The practitioners of the parent discipline instinctively resent the contraction of their territory. The interests of the new specialty often conflict with the aspirations of other fields that have been newly created. The need for the very existence of new branches is often questioned. All these historical conflicts have afflicted the birth and growth of vascular surgery.

Everyone knows about "heart disease", but very few know about vascular diseases. Infact vascular disease kills and cripples almost as many Indians as heart disease or cancer. The sheer magnitude of the problem of vascular disease in India is staggering. Although there is no accurate vascular registry, the fact that there are over 25 million Diabetics in the country is just a small pointer to the vast numbers of the undiagnosed vascular cases. Patients of severe vascular disease have been treated for low backache and arthritis for years. It is only the onset of peripheral gangrene which brings to light the fact that arterial pulsations have been absent for long periods of time hitherto unnoticed. After diagnosis also the only treatment of these unfortunate cases has been amputations leaving the primary vascular problem unsolved. The lack of awareness of the disease is so acute, that even some cardio-vascular surgeons have never heard of a separate, independent vascular surgery department or a vascular surgeon. A truly tragic situation indeed!

From the beginning, the existence of independent vascular surgery as a specialty was challenged by the Medical Council of India, as in India it still considered to be the part of the broad speciality of "cardio-thoracic-vascular surgery' (CTVS). To the exception Medical Council of India has granted Madras Medical College, Chennai to start the MCh training programme in vascular surgery, but unfortunately the facility can only be availed by the surgeons of the state, thereby denying valuable training opportunity to the surgeons from rest of the country. However, all the hope is not lost for the vascular patients of India. Thank's to the effort of National Board of Examination, New Delhi, which understood and realized the magnitude of the problem. With a vision and mission in 2001, the National Board of Examination started a two years fellowship programme in peripheral vascular surgery and hence giving a separate independent recognition to this subject. Presently this course is available in only three major cities and needs further expansion in future to cover the entire country.

Inspite of this still the picture is not clear. Cardiac surgeons in India still claim themselves to be the best vascular surgeons also. No matter, as in reality there operative vascular work is less than 2% and there CTVS training is skewed only towards cardiac surgery. Infact the approach, diagnosis and therapy of vascular diseases is very much different from approach to a patient with heart disease. No doubt that cardiac surgeon is technically very competent to perform vascular operations, but they are universally burdened with coronary bypasses and valve replacement. So no reason to blame them, infact what is required is a separate recognized vascular surgeon who can take care of the peripheral vascular system.

Not only that, to confuse and complicate the issue further we now have general surgeons, thoracic surgeons, general surgeons with some experience in vascular surgery, and general surgeons with added qualifications in vascular surgery all performing the full assortment of vascular operations. This conceptual puzzle kept many hundreds of surgeons in resentful confusion for years. Time, however, slowly but surely is beginning to sort out this confusion: hospitals concerned with their professional standing are increasingly inclined to grant vascular privileges to new staff members only if they are certified by the Medical Council of India or National board of Examination as having special or added qualifications in general vascular surgery.

The image of the vascular surgeon is gradually acquiring formal recognition, but the limits of the legitimate participation of the general surgeon in treating vascular diseases in actual practice, is still very high in the real scenario.

As this problem of identity is being yet to be solved, vascular surgeons face other problems that impinge on their practice. Now even cardiologists and radiologists are also claiming themselves in the race of treating and eliminating vascular diseases. A real challenge indeed for the vascular surgeons!

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sets an agenda for change – a change for health development in the twenty-first century, better performance, financing of healthcare, continuous quality improvement, strategic planning, global reforms, political intricacies, constraints and concern – a conceptual revolution in the mindset of the people in general and health professionals in particular. It contains current topics/recent advances in medicine and technology including Human Genome, Biomedicine, Stem Cell Research, Human Cloning, E-Health, Telemedicine, Environmental health, Global Health Threats, SARS, AIDS, Emergent Infection, Health research, Bioinformatics, Endangered future of humans, RCH, Mental Health, Legal aspects of health care, Medical ethics, Future trends in healthcare, etc. The aim of this book is to re-examine the central problems relating to health and healthcare, to evaluate the significant breakthroughs, to assess the effectiveness of national policies and to stimulate the development of new national strategies for the public health – how the nation might best re-establish its pre-eminence in the pursuit of public health.

Hospital Infection Control: Conceptual Framework
Academa Publishers
2005 300pp. Rs. 250

This book is designed as a text that not only explores the basics of hospital acquired infections but also answers many of the frequently asked questions about its prevention and control. It has also been designed to develop the readers understanding beyond implementation. It sets out to present the fundamentals of hospital infection, explore understandings, examine new and emerging issues, current challenges in the field, and suggest ways of dealing with some of the many concerns. This book is a vital resource for medical undergraduates, postgraduates, medical teachers, clinicians, hospital administrators, nurses and other health professionals to enhance the knowledge and capabilities of health professionals of all disciplines.

Forthcoming Books

- Fundamentals of Problem Based Learning
- Essentials of Disaster Management

Born in a small Village ***Magam, Tehsil Handwara (J&K), Dr Asadullah Lone*** *received primary education in Magam till 7th. Class in the "Middle School", Handwara. Did his next three Classes from Hari Singh National High School Baramullah (J&K). Constituted the last Batch from SP Colege, Srinagar, attached to the Punjab University, Lahore for his FSC degree . Left for Pakistan at the age of 17 years to join King Edward Medical College, Lahore, in 1948. Completed MBBS in-1953, DLO in 1955 and MS in 1962. Was the first teacher of ENT to Liaquat Medical College Hyderabad Sind (Pak) in 1956 and the first registrar in ENT at Myo College Lahore. Held various posts (See below) and retired as dean PGMI Lahore In September 1990. Recalled by the Government of Punjab (Pak) December 1998 as member Public Service Commission.*

Dr. Asad Ullah Lone visited Kashmir in 1970 after having left in 1948 his subsquents visits to this place were in 1985 and 2001.

Name :	**Dr. ASAD ULLAH LONE**
Date of Birth:-	9-September, 1930
Address:-	17A, Model Town, Lahore, Pakistan

Educational Qualifications;

- MBBS — King Edward Medical College, Lahore
- DLO — Punjab University, Lahore
- MS — Punjab University, Lahore
- FCPS — Pakistan College of Physician & Surgeon, Kasulli

Training Abroad

- Columbo planfellowship, NewSouthWales, Australia(1960-61): As reseach registrar. Work thesis on Surgery of Deafness.
- Columboplan fellowship University of Toronto (Canada)1969-Surgery of the Ear, Labrynthin Physiologyand Audiology

Special Interest: Micro-otology

Posts held:

- Professor ENT
  Multan Medical College
  Fatima Jinnah College for women Lahore
  King Edward Medical College Lahore.
- Dean Post graduate Medical Institute Lahore till September 1999.

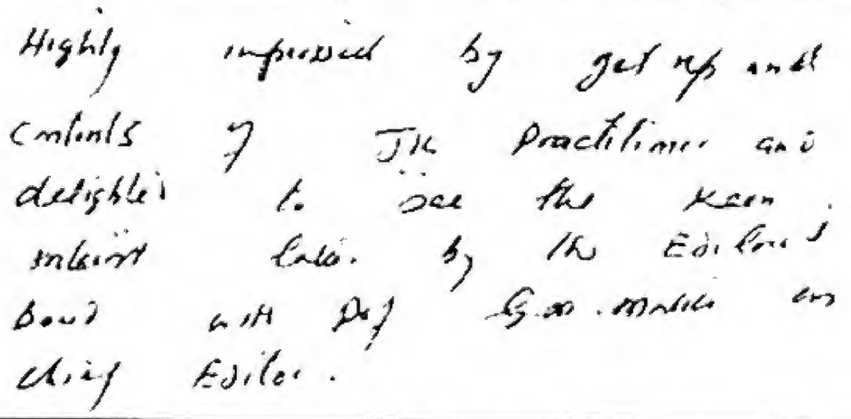
Other Positions:-

- Served as Member Punjab Public Service Commission (Pakistan) on a three year contract from 11-12-1998 to 10-11-2001 and latter as chairman.

Academic & Other Activities:

- Member Pakistan Medical and Dental Council (PMDC)(1987-1990)
- Member Board of Studies in Medicine Punjab University Lahore (1988-1998)
- Chancellor Pakistan College of Physician & Surgeon. Lahore (1988-1998)
- Supervisor of FCPS –Fellow College of Physician & Surgeon (ENT)
- Examiner ENT both at Underguade & post graduate level

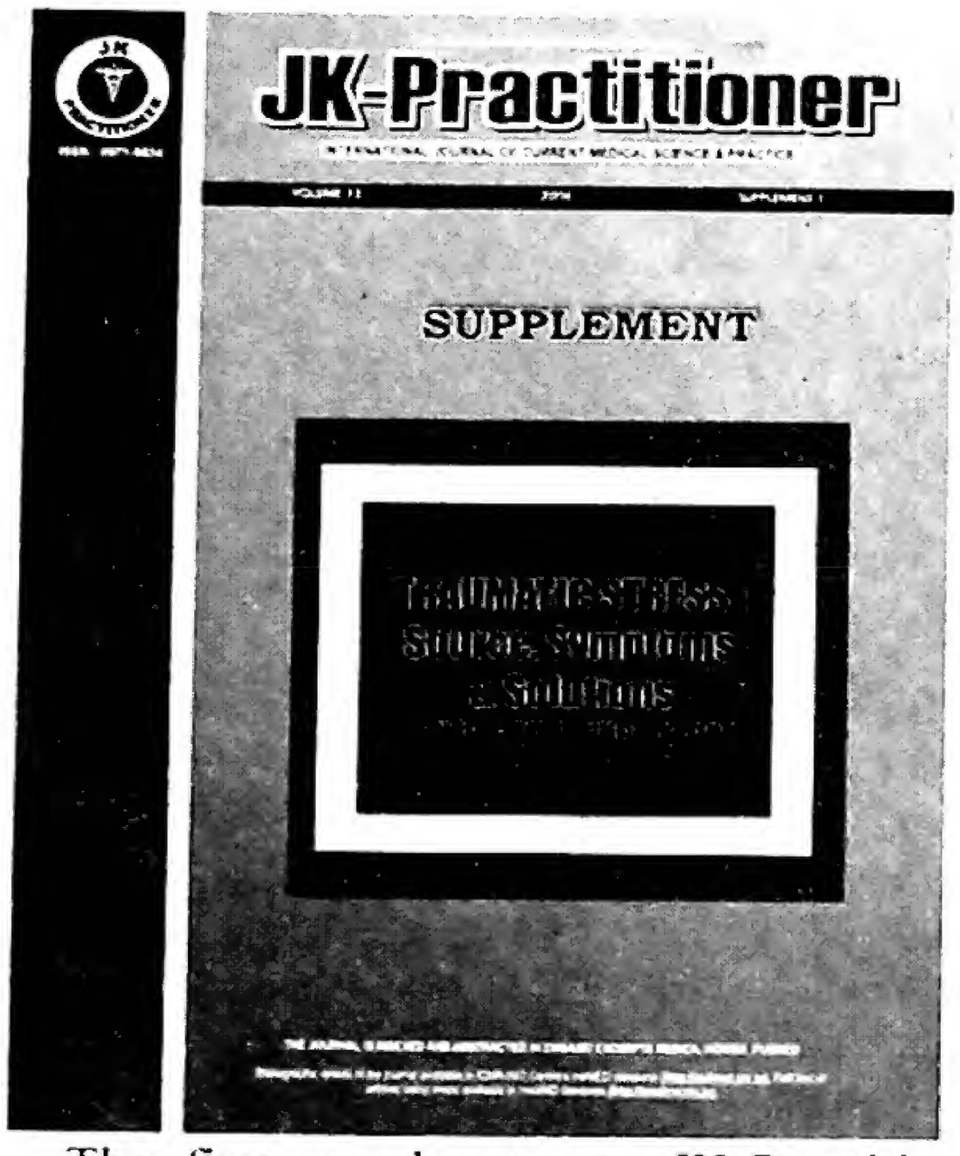
During his last visit to Srinagar he had this to say about JK-Practitioner-



As we go to the press we hear the sad news of the demise of Dr. Asad Ullah Lone. The Editorial board of JK-Practitioner deeply condone the death of this eminent personality. May his soul rest in peace. Prof. Mohd. Lateef HOD ENT & Head and Neck Surgery Govt. Medical College Srinagar & his Collegues in the Deptt, also express heart felt Condolances on the denise of Dr. Asadullah Lone.

The First Supplement to JK-Practitioner

Traumatic Stress:Source Symptoms & Solutions.
South Asian Experience
Supplement to Jk-Practitioner.
Supplement 1 Volume 13, 2006



The first supplement to JK-Practitioner is published. We are encouraged to see the overwhelming response to this publication from the scientific community. Within no time, the request by the National center for PTSD (USA) to index and abstract its contents in the PILOTS Database has been a sense of pride for the editors. The National Center has emerged as the world's leading research and educational center of excellence on PTSD and the PILOTS database is their online index to the world psycho trauma literature

The leading lights in Psychiatry both domestic and International have pleasant words for us.

The supplement presents the research carried out by Dr.Mushtaq A Margoob (Guest Editor for the issue) and his colleagues on various aspects of Traumatic Stress. Traumatic stress has its various forms and can victimize anyone, be it a child, an adult or the doctor himself..Dr.Magroob's inroads into these various dimensions of this disorder is thought provoking and should go a long way in our understanding and management of post traumatic stress and disorders related to it. This scholarly document should prove of immense help to the researchers ,doctors,mental health professionals, policy makers and social scientists. Fulltext of articles are available online at www.medind.nic.in

Zaffar Abbas Khatib MD
Executive Editor,JK-Practitioner
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US Department of Veterans Affairs
National Center for PTSD

Dear Dr. Abbas,

We were delighted to receive the recent supplement to JK-Practitioner devoted to "Traumatic Stress : Source, Symptoms & Solutions : South Asian Experience". We are in the process of indexing its contents in the PILOTS Database, our online index to the worldwide psychotrauma literature. To facilitate this, are you able to provide us with the article abstracts in electronic form, or direct us to an online source for them ?

Many thanks,

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Australian International Health Institute

AIHI

Dr Mushtaq A Margoob
Associate Professor
Department of Psychiatry
Government Medical College, Srinagar
P O Box No. 711
GPO Srinagar, Kashmir
INDIA

9 June 2006

Dear Dr Margoob

Thank you for sending me the supplement issue of the *Jk Practitioner* with yourself as guest editor. Congratulations on editing this excellent and inspiring series of articles. This is the finest experience of the work that provides the way forward.

I hope to see you soon and wish you well continuing your work.

With kindest regards,

Helen Herrman
Director of Academic Programs
Australian International Health Institute
Director, WHO Collaborating Centre for
Research and Training in Mental Health
Professor in Public Health and Psychiatry
The University of Melbourne

Building Partnerships for Health Development

Dear Dr. Margoob

Thanks a lot for sending the supplement issue of the JK-Practitioner. I amazed to see the high quality of the Journal and high standard papers. I have the notion to send my article to this high impact Journal.

I would be happy if I get the issues of the Journal regularly, preferably to my home address as mentioned below.

Please keep in touch. Thanks again for the Journal. Hope to meeting you in future in an occation.

With best wishes and regards.

Dr. Mohammad S I Mullick
MBBS, MRCPsych (London), FCPSPsych, DCAP (London)
Associate Professor of Child and Adolescent Psychiatry
Department of Psychiatry
Bangabandhu Sheikh Mujib Medical University
Dhaka 1000
Bangladesh
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Dear Dr. Margoob

Many thanks for Supplement issue of trauma of JK-Practitioner. It is for this reason I wanted you to come and speak in Luchnow during the November 2005, IACAM conference.

With best wishes,
Your Sincerely,

Prabhat Sitholey
Deptt. of Psychiatry
K.G. Medical University
Lucknow

Dear Dr. Mushtaq A·M

Thank you very much for sending me a copy of the supplement - traumatic stress of the esteemed Journal JK-Practitioner, you as the guest editor of the supplement.

It makes a good academic reading loaded with information, respond findings for the various dimensions of a current universal problem of post traumatic stress disorder. Please accept my hearty congratulations on your committed effort on the topic. A research work of this order coming from J&K is all the more commendable. I wish you keep up research interest & come out more on different aspect of Human Behaviour.
Wish you all the best.

Thanking you,
Yours Sincerely,

Dr. S.M. Channabasavanna
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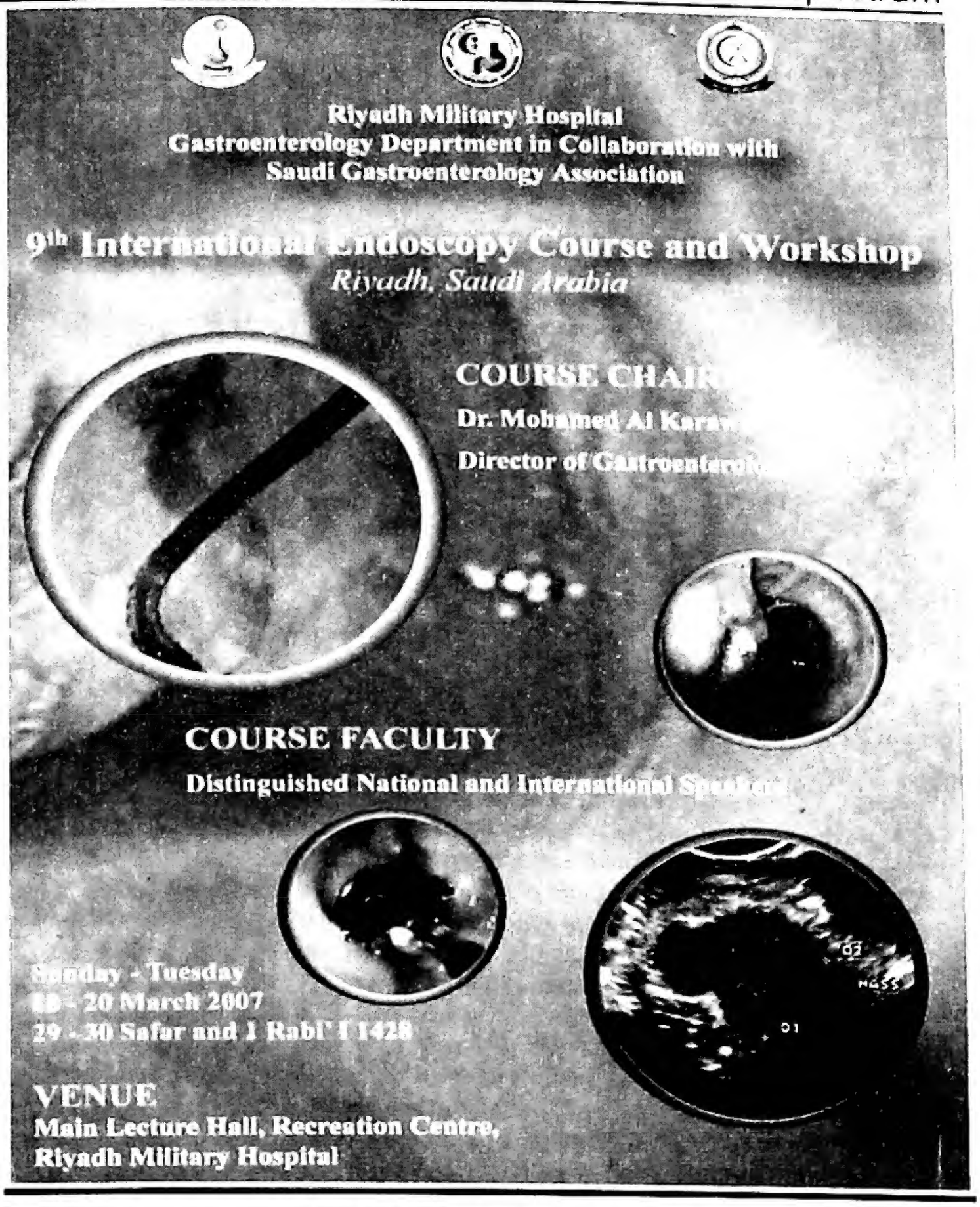

JAIPUR

36TH ANNUAL CONFERENCE OF ENDOCRINE SOCIETY OF INDIA 17th, 18th & 19th NOVEMBER, 2006

THEME: CLINICAL ENDOCRINOLOGY IN THE ERA OF MOLECULAR REVOLUTION

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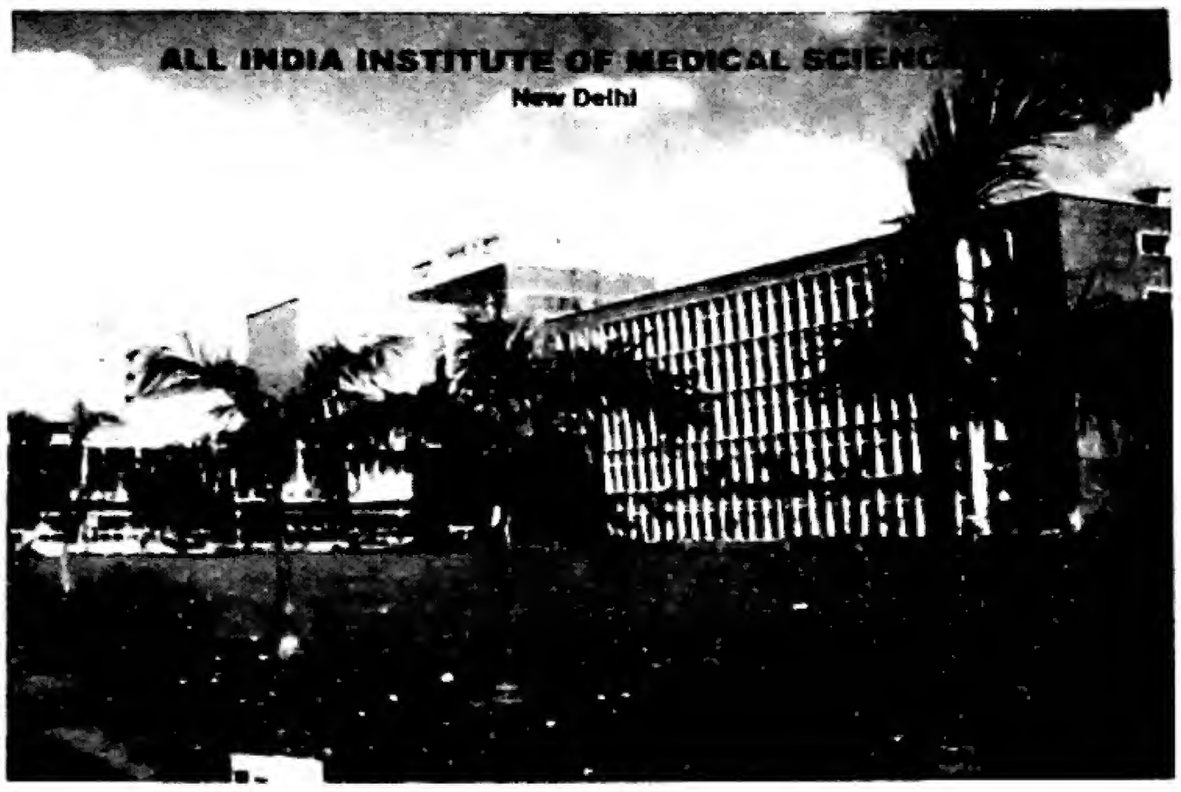

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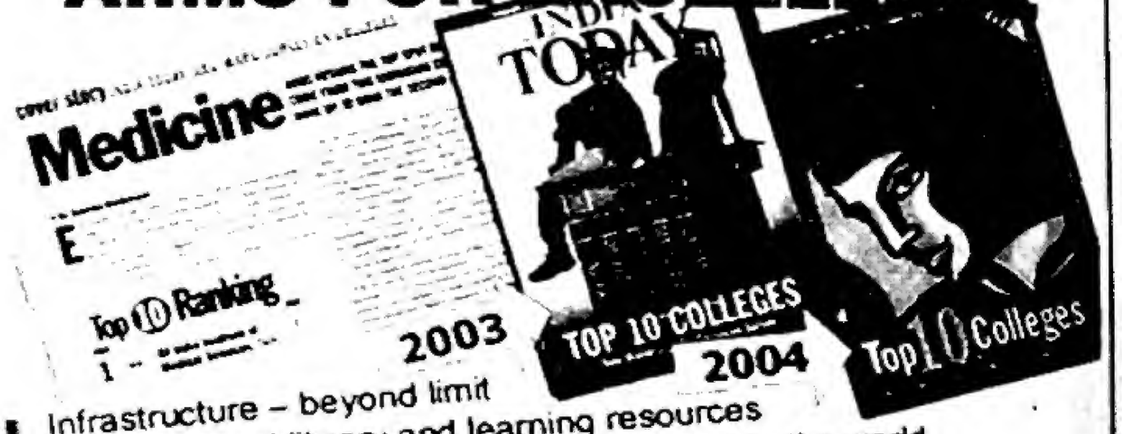

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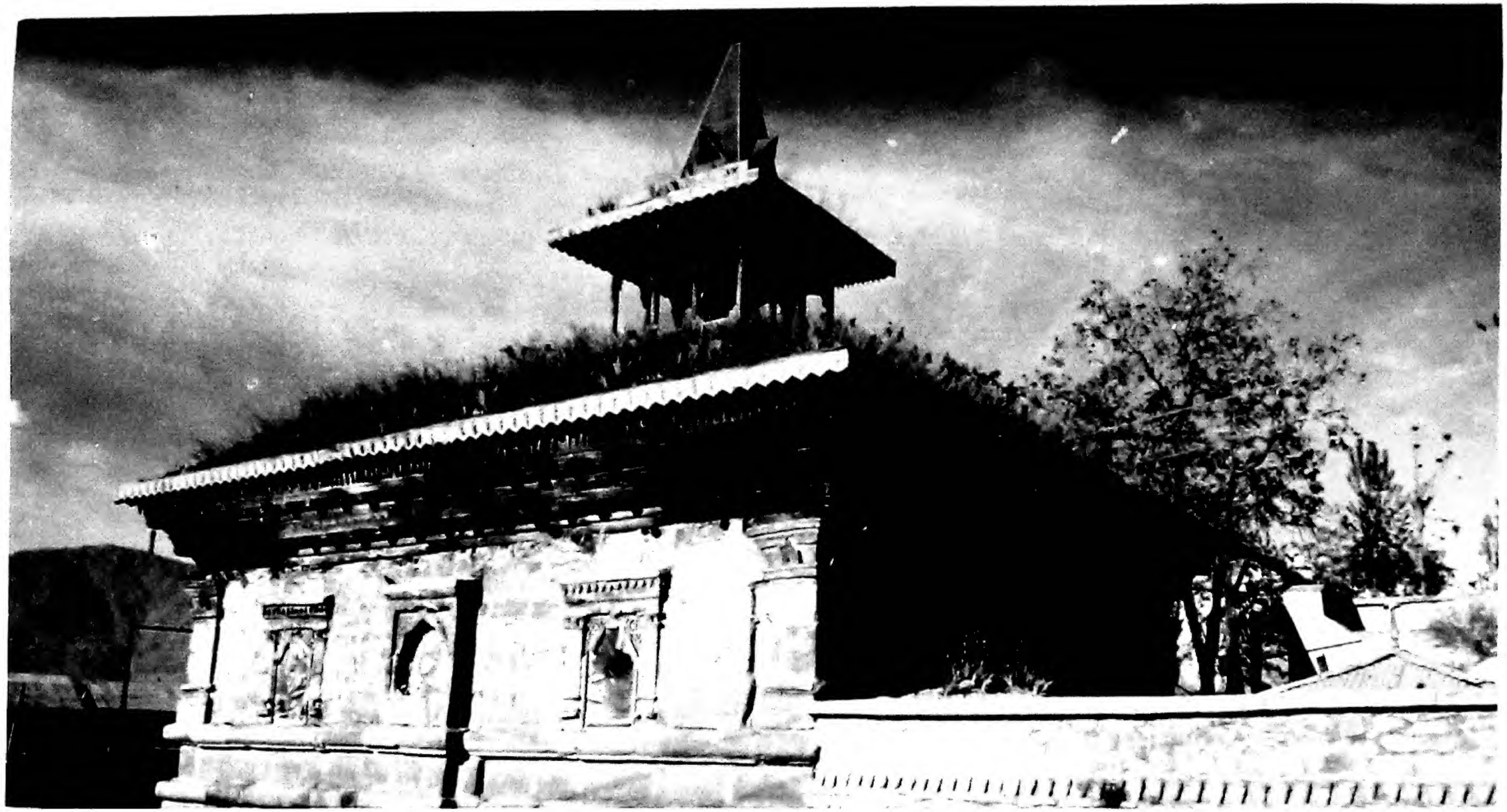

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(ii) Benign acute childhood myositis; resentation and management in emergency. **JK-Practitioner2006:13 (3):149-150.** Read **Javeed Iqbal** as an author after **Parvez Ahmad.**

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Colour Doppler of Abnormal Liver Circulation

Feroze Shaheen, Tariq Gojwari, Manjeet Singh, Riyaz Rasool, Hamid Hussain Banday.

In tandem with advances in grey scale ultrasound like tissue harmonic imaging, colour Doppler has had tremendous force-multiplier effect in detecting hepatic diseases especially those of heamodynamic nature, obviating need for invasive vascular procedures with their attendant risk of morbidity and mortality.

Colour Doppler is based on the principles of colour coding of the frequency shifts which occur with blood flowing towards or away from a transducer. The frequency shifts can be converted into velocity measurements and audible sound simultaneously giving a real-time scene and sense of changing heamodynamics.

Two most common vascular disorders affecting liver are portal hypertension and hepatic venous obstruction. Other less common lesions like hepatic arteriovenous fistulas, aneurysms and vascular tumors etc also lend themselves easily to interrogation by colour Doppler.

Portal hypertension:

It can result from increased resistance (most common) or increased flow. In either case there is enlargement of extrahepatic portal vessels and opening up of spontaneous porto-systemic collaterals.

Various grey scale measurements suggesting enlargement of portal veins vary from 10mm (Webb et al[1]) to 17mm (Cottone et al[2]), varying with the populations studied and the stage of the disease even though some authors have reported patients with alcoholic cirrhosis where despite presence of large collaterals, portal vein measured between 10-12 mm[3]. The same applies to measurements of splenic and superior mesenteric veins which also vary from one series to other with some authors like Weill suggesting that a caliber of splenic vein of 20mm or greater be considered a specific sign of portal hypertension[4].

Loss of normal respiratory phasicity in splenic and superior mesenteric vein is relatively more specific sign of portal hypertension[5], as the increased intrahepatic resistance minimizes dilatation of portal vein during Val Salva's maneuver.

Doppler not only clarifies doubtful real time images but also provides new insights e.g in chronic portal vein thrombosis when the portal vein is small and reflective, Doppler of portahepatis reveals no evidence of blood flow. Colour Doppler best demonstrates the continuous low velocity flow when cavernous transformation of portal vein has occurred(fig 1). Similarly partial thrombosis appears as absence of colour signal even when the thrombosis is anechoic(fig 6). In some cases, Doppler ultrasound is more accurate than arterioportography which can erroneously suggest portal vein thrombosis when there is reverse flow in a patent portal vein[6]. In one series 5-8% of patients with portal hypertensions had reversed flow[7]. Hepatofugal flow is associated with decreased risk of variceal bleeding, however it doesn't predict survival[8]. Hepatofugal flow in splenic vein has proved to be closely related to hepatic encephalopathy. The reversed flow is easily detected in colour and spectral doppler when the colour in vessel is reversed and spectral trace lies below the baseline. The heamodynamic response to elevated sinusoidal pressures results in reduction of mesenteric arterial pressure thus maintaining the portal hypertension. The dilatation of intestinal arteriolar bed results in decrease in pulstality index in SMA and is closely related to development of varices[9]. (fig 4,5).

In parallel with these effects there is increase in hepatic arterial impedance indices correlating with increase in sinusoidal resistance[10].

The portal flow volume can be measured by multiplying time averaged mean velocity calculated from mean doppler shift and cross sectional area of the vessel[11]. However certain guidelines have to be followed to maintain the accuracy and reproducibility of portal blood flow measurements like sample

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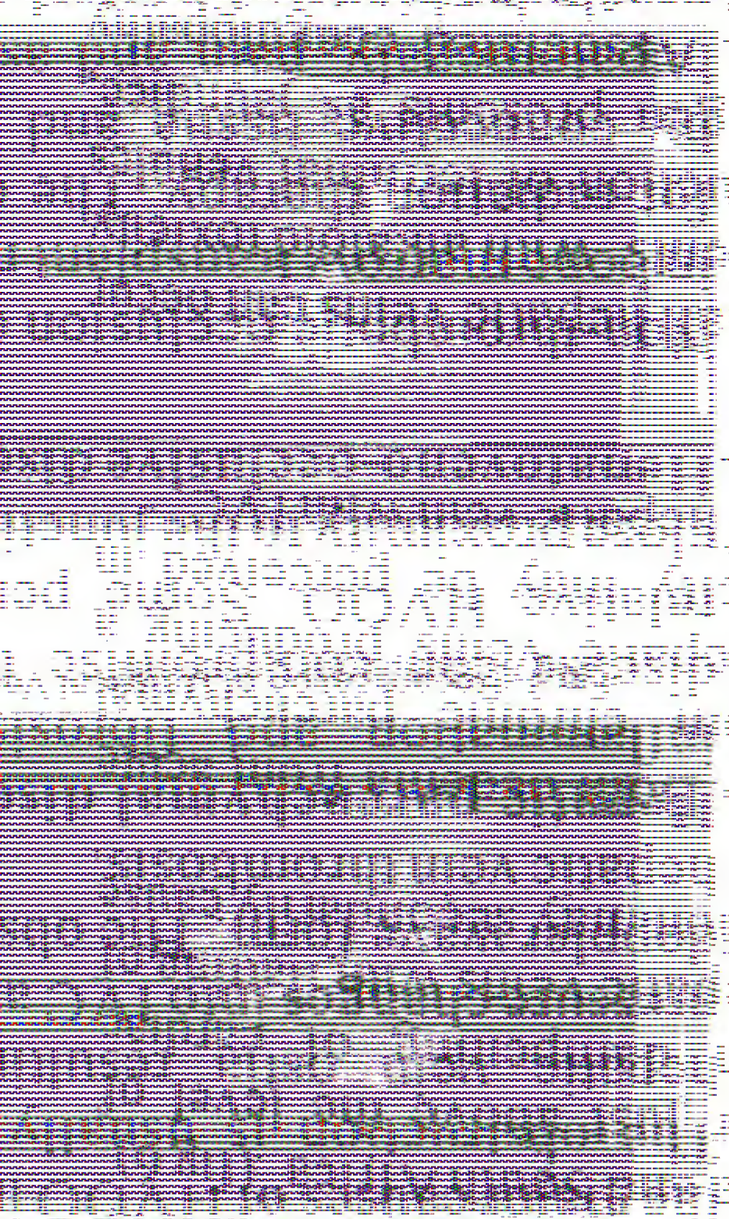

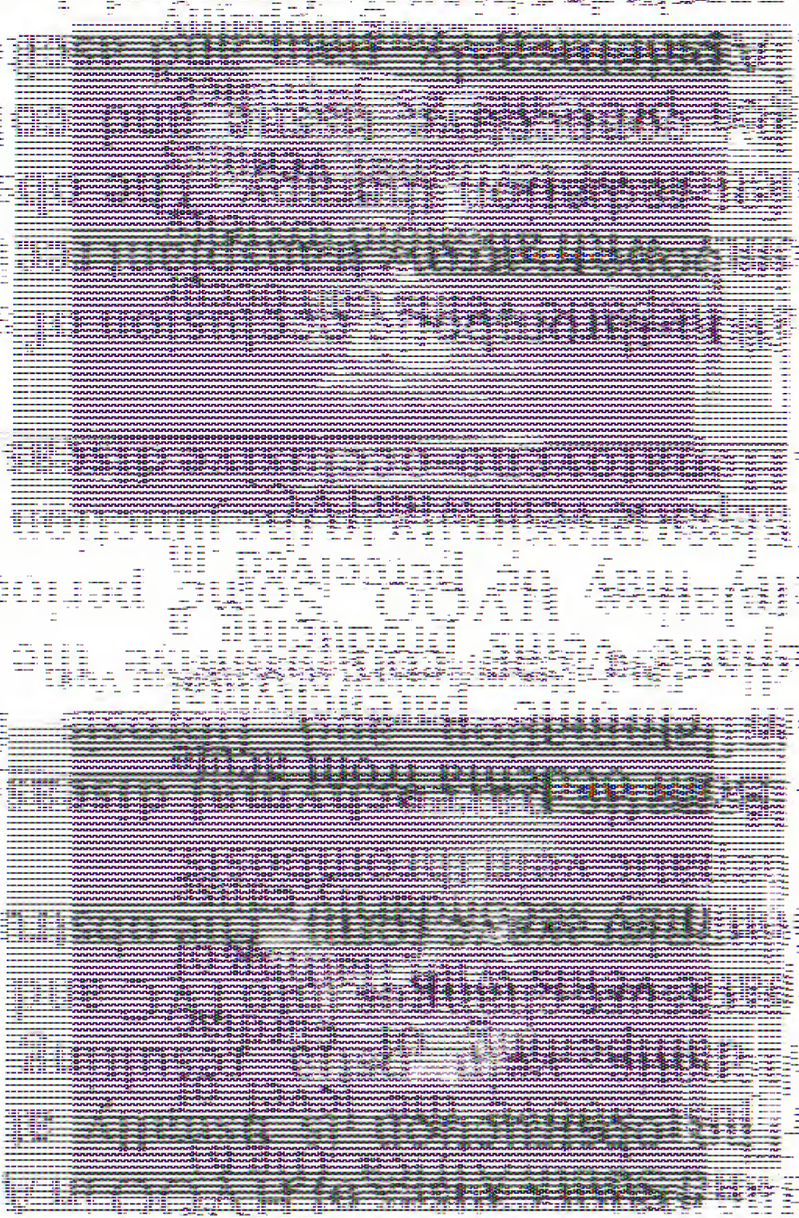

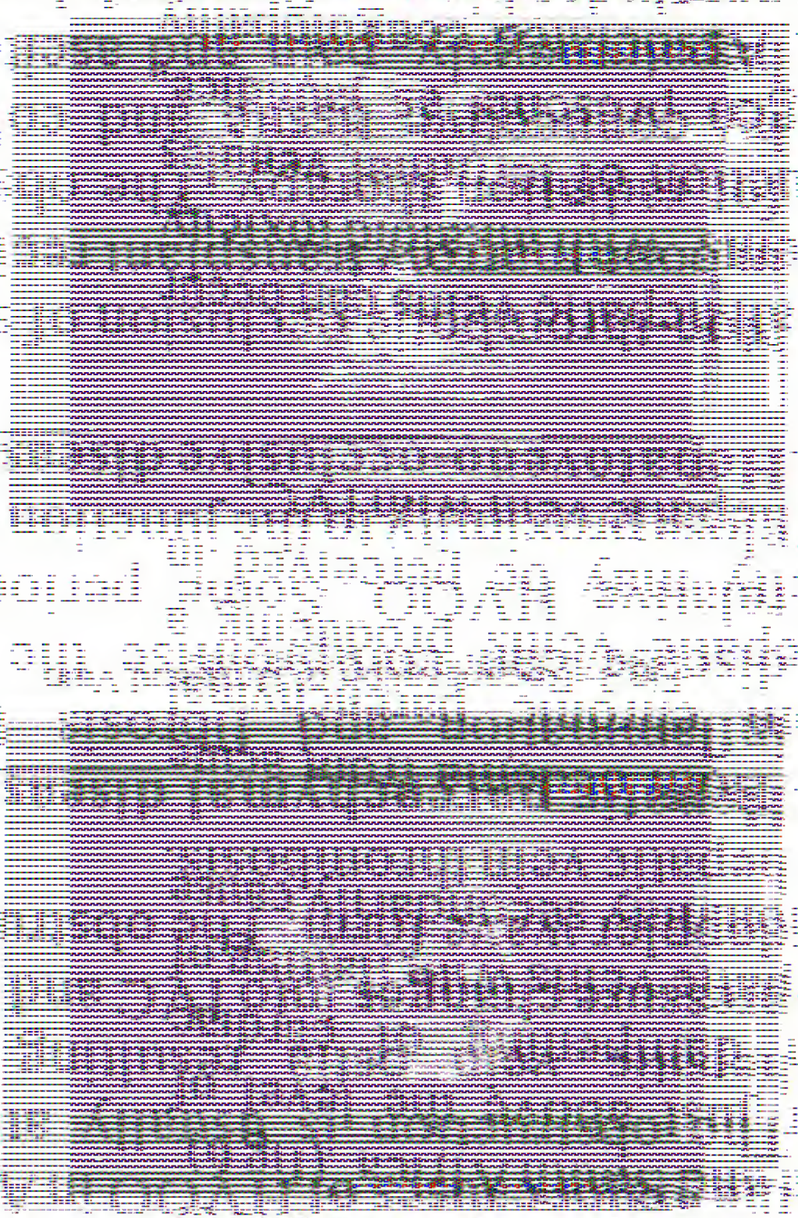

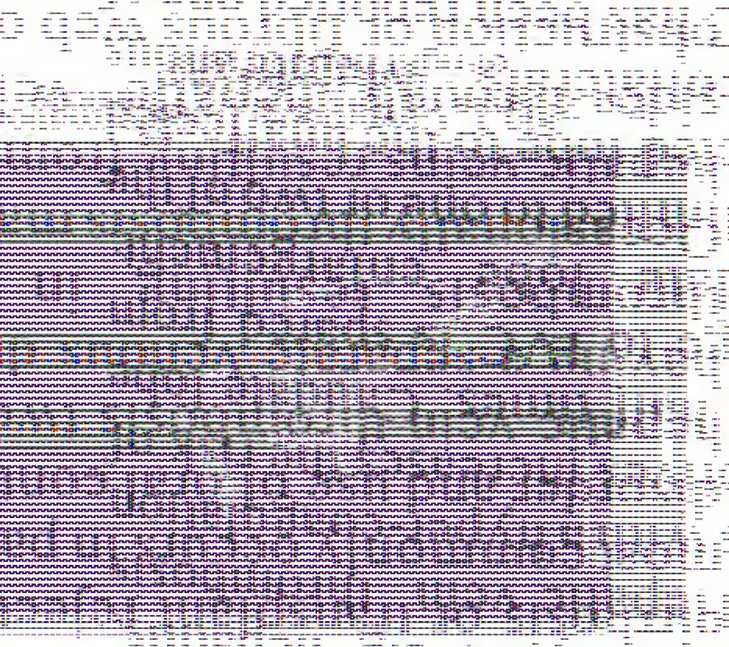

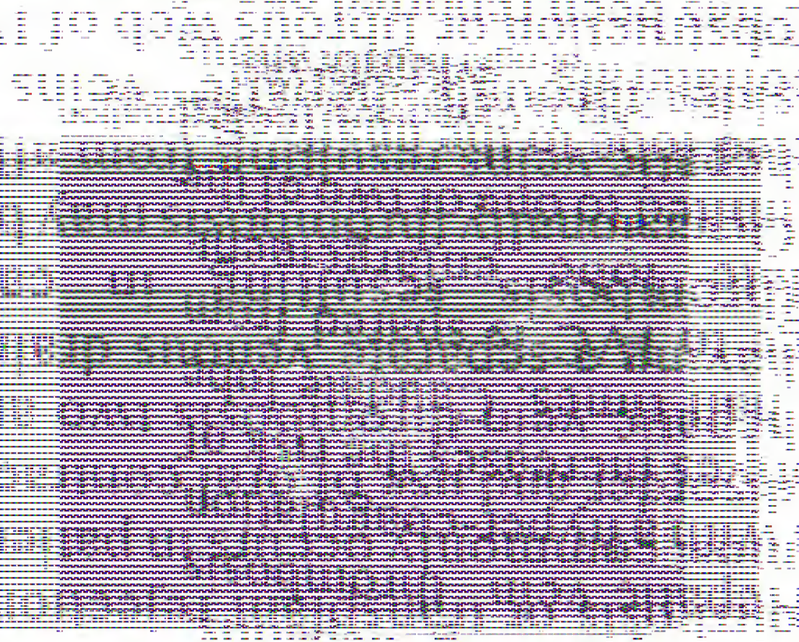

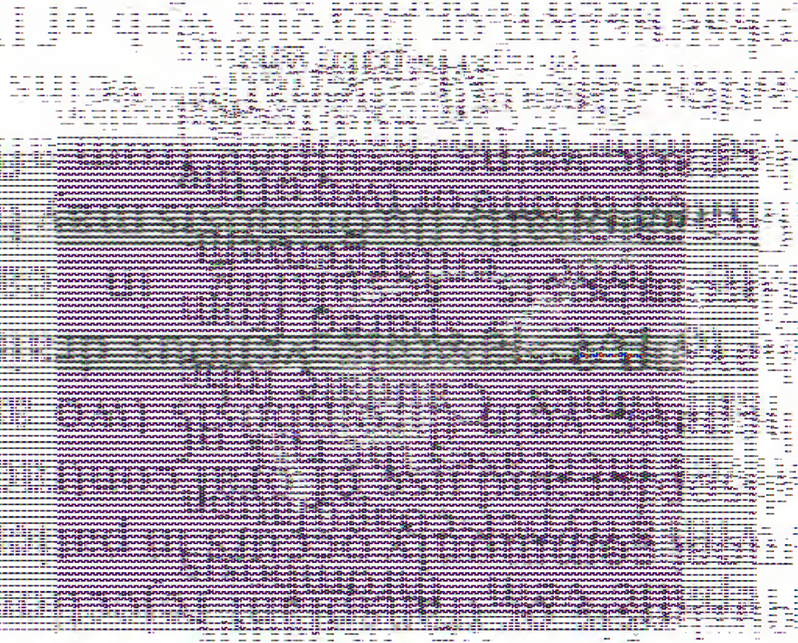

arterio venous fistula. Spectral doppler profile show bounding arterial inflow velocity, swirling turbulence flow within the aneurysm and arterialization of venous outflow[21]

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Small bowel obstruction in children – A surgical challenge

Zahur Hussain , Khurshid Ahmad Sheikh, Reyaz Lone, Sajad Arif, Ashuffa Rasool, Syed Mudassir, Abdul Rouf Khawaja , Ab. Wahid Mir, Nasir Wani.

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Introduction

The small bowel is a marvel of complexity and efficiency. Amongst the disease processes involving the small bowel, obstruction still represents the most difficult and vexing problem that a surgeon faces[1,2]. Correct diagnosis, optimal timing of therapy and the appropriate treatment are very challenging. One should embrace the philosophy of "Never let the sun set or rise" towards treatment for the patients with small bowel obstruction. Though the knowledge of this dreadful malady dates back to antiquity, it still taxes the diagnostic ability and clinical judgment of a surgeon to a very high degree[3,4]. In fact there are very few problems in surgical physiology, which have earned greater attention than those associated with intestinal obstruction[24]. Intestinal obstruction is responsible for approximately 20% of surgical admissions for acute abdominal conditions[5,7]. The small bowel is involved in 60-80% of cases of intestinal obstruction[6]. In spite of advances in imaging and a better understanding of the pathophysiology of the small bowel, it's obstruction is still frequently misdiagnosed[7]. Despite advances in the treatment of this condition the attendant mortality is still high and remains in the range of 5% to 11%[8].

Small bowel obstruction is a common problem seen in children of Kashmir. Most of the cases are because of worm (ascariasis) obstruction[9,10,11,12,13]. Group of patients who report with ascaridial obstruction are very alarming and challengeable for the surgeon because of fear of strangulation and intestinal gangrene and their migratory habit and tendency to explore orifices and ducts leading to a variety of other dangerous complications and poor prognosis[11,14]. So this problem cannot be ignored while treating the cases of small bowel obstruction.

In a society like ours, most of the children admitted with mechanical small bowel obstruction are from rural areas who usually present late because they are either mismanaged in peripheries and referred to us late or they report late because of ignorance and illiteracy and usually present as complicated intestinal obstruction. So it is the need of hour to avoid this dreadful condition to occur, and manage these cases at the earliest.

Types of obstruction:-

Small bowel obstruction is mainly of two types[2,15,16]. Mechanical or Dynamic obstruction and Functional or Adynamic obstruction. Mechanical obstruction means that luminal contents cannot pass through the gut tube because the lumen is physically blocked or obstructed, whereas functional obstruction means that luminal contents fail to pass because of disturbances in gut motility that prevent coordinated transit from one region of the gut to the next. This latter form of obstruction is commonly referred to as ileus or pseudo-obstruction[15].

Causes:-

Small bowel obstruction is the commonest surgical emergency encountered in childhood[17,18] ranks high in importance as an acute surgical catastrophe in infancy and early childhood. The pathological leading points such as polyps, Meckel's diverticula and intestinal duplications are seen in 5% of the total number of intussusceptions[19].

Volvulus[20,16] of the small intestine is an infrequent cause of small bowel obstruction. It usually occurs in the lower ileum, and is favoured by the presence of an adhesion passing from the antimesentric border of an intestine loop to the parieties.

Adhesions[21,22] (postoperative or postinflammatory) causing intestinal obstruction are not infrequently encountered in pediatric surgical practice. However, some intestinal obstructions result from bands that are

not the remnants of described embryologic structures and do not show an association with a previous intraperitoneal insult. Postoperative adhesions giving rise to intestinal obstruction usually involve the lower ileum. The risk of developing an adhesive small bowel obstruction is greater when there was more than one prior peritoneal procedure, and when, during this prior procedure, there was already peritonitis. In the literature, there is disagreement about the frequency of postoperative mechanical small bowel obstruction in children[22].

Hernias[23] give rise to intestinal obstruction when incarcerated. In children inguinal hernias are commonly obstructed and there are high chances of strangulation or intestinal gangrene. The postoperative complication rate is more than 20% in incarcerated cases as compared with 1 to 2% in elective procedures.

Ascaris lumbricoids is the most common intestinal parasite encountered in India[6]. Worm obstruction due to Ascaris lumbricoides is one of the most common causes of intestinal obstructionin children, usually under 10 years of age[10]. Ascariasis remains a formidable problem in India, as a study has shown that stools of more than 70% of children have round worm ova[24]. In the Kashmir valley, the incidence of ascariasis was observed as 85.1% of the total helmenthic and protozoal infected cases. It affects mainly children from rural areas, low income groups whose standards of public health and personal hygiene are at the lowest[10,24,12,13]. It is the big mass of worms which causes mechanical bolus obstruction in the small bowel[25,14].

The less frequent causes of small bowel obstruction in children include congenital cysts (e.g. enterogenous cyst) and tumors (e.g. non-Hodgkin lymphoma).

Although the exact incidence figures are not available, there is probably not a day that goes by in which any busy clinical abdominal surgeon does not at least once consider a possible diagnosis of small bowel obstruction.

Symptomology :-

The cardinal symptoms that characterize mechanical small bowel obstruction include abdominal pain (colicky), vomiting, abdominal distension and obstipation (failure to pass flatus and faeces)[2,15,16]. Initially pain tends to be diffuse, poorly localized, episodic and crampy in nature. However with the onset of bowel ischemia pain becomes constant. Vomiting occurs early in proximal small bowel obstruction but may be absent or develop late in distal obstruction. Character of vomitus also differs as far as the site of obstruction is concerned. It is bilious in high obstruction and can be feculent in distal obstruction. Visible peristalsis may be seen in thin patients while in others distention may be prominent which is usually centrally placed. Abdominal auscultation usually reveals periods of increasing or crescendo bowel sounds with the abnormal bowel borborygmi of tinkles, splashes and rushes that coincide with the abdominal colic.

Investigation :-

In addition to a very careful and thorough history and physical examination, all patients require baseline laboratory studies, including a complete blood count, serum electrolytes, and a flat and upright plain film of the abdomen, as well as any other specific tests that might be suggested by the patient's history or concomitant medical problems[2,1,16]. Plain radiograph of the abdomen is an important diagnostic too. The cardinal findings include dilated loops of small intestine on the supine radiograph and multiple air-fluid levels, which often layer in a stepwise manner on erect radiograph or lateral decubitus film. In general, dilated loops of small intestine are defined as those larger than 3cm in diameter[15]. When doubt remains contrast studies of the gastrointestinal tract, USG & CT can help in diagnosis.

Patients with partial small bowel obstruction may be treated conservatively with resuscitation and tube decompression alone[26,27]. In general the patients with complete small bowel obstruction require operative intervention[28].

Certain criteria have been proposed for the surgical intervention in patients with intestinal obstruction (esp. ascaridial obstruction), the two important being- Dayalan's & Louw's respectively.

Deciding about surgical intervention:-

A casual perusal of the literature of antiquity suggests that bowel obstruction and its poor outlook were known to the ancients. Persistent vomiting accompanied by pain and abdominal distention were treated by Hippocrates with enemas and inflation of the rectum by means of a bladder attached to a pipe[18]. The earliest reasonable authentic report of operation for intestinal obstruction is that of Praxagoras (3rd to 4th century B.C.) who created an enterocutaneous fistula to relieve obstruction[25].

Until the late 1800s, non-operative management of these patients was the rule. In publishing his prize winning monograph of 1899, Frederick Treves included such conventional procrastinating treatments as posture and taxis, opium, purgation (a measure he least supported), administration of metallic mercury, electricity, enemas, and inflation of the bowel with water, air and other gases. He listed, without endorsement, puncturing the bowel with a fine needle or trochar and mentioned too, the more dangerous procedure of enterocentesis, in which the trochar and needle is left in the bowel for varying periods of time for temporary decompression or with the hope of establishing an external fistula[3].

In the 19th century, surgical procedures became more frequent for intestinal obstruction. The 2nd decade of the 20th century saw the development of radiographic techniques for the diagnosis of intestinal obstruction. The 1930s marked a beginning of the new era in the management of intestinal obstruction with the application of suction to indwelling gastroduodenal tubes. Antibiotics were employed to the treatment of intestinal obstruction in 1940s and 1950s[3].

The rapid scientific advances made after the first and second World Wars led to a better understanding of the pathophysiological aspects of intestinal obstruction and in turn to the concept of the rapid correction of patients physiologic deficits before any surgical intervention. The result was a decrease in the mortality but since then, the problem of morbidity remains unresolved despite a satisfactory decrease in the mortality. That intestinal obstruction is due to multiple causes has been established by many studies[1,17,3,29]. Furthermore, major causes of

intestinal obstruction vary from country to country and at times within smaller geographic areas[1].

The modern day surgical management of small bowel obstruction continues to focus appropriately on avoiding operative delay whenever surgery is indicated. "Frederic Treves" of the London Hospital, in his monograph of 1899 said, "It is less dangerous to leap from the Clifton Suspension Bridge (250-275 feet above the Avon River) than to suffer from acute intestinal obstruction and decline operation"[5]. The wisdom of the adage "never let the sun set or rise on a small bowel obstruction" remains a most practical guideline whenever any uncertainty exists[1].

The most important complication, which has been constantly bothering the surgeons, in intestinal obstruction, is strangulation, when the urgent surgical interference becomes mandatory, but it is not always possible to decide preoperatively about the presence or absence of this gruesome complicaiton,[31,28,32]. The high mortality rate associated with this jeopardized vascularity of the gut is quite well known.

Prompt recognition of the need for operative intervention when clinically indicated remains the cornerstone of the modern day surgical management of acute small intestinal obstruction.

Louw (1966) ; studied the abdominal complications of Ascaris lumbricoides infestation in children aged 1 – 12 years. He found intestinal obstruction as the commonest complication (in 68 out of 100 patients). In the majority of cases the obstruction was incomplete and responded to conservative therapy, but in about one-sixth there was complete occlusion or strangulation due to intraluminal blockage, intussusception, volvulus or associated bands. In 2 cases worms per se caused necrosis of the intestinal wall. He concluded that the treatment should be conservative in the first place, but laparotomy should be performed in the following circumstances:-

a) The passage of blood per rectum.
b) A very ill child with tense abdominal distention and rebound tenderness.
c) The presence of multiple fluid levels on abdominal radiographs.
d) Unsatisfactory response to conservative therapy.

He also concluded that the worms should be dispersed without opening the bowel, but there should be no hesitation to resect bowel when necessary.

Dayalan et al (1976) ; studied the pattern of intestinal obstruction with special preference to ascariasis. The study comprised of 2295 cases of intestinal ascariasis studied retrospectively for nine years. Out of these 2295 cases 159 (7%) were classified as having ascaridial obstruction. Some guidelines for recognition of failure of conservative management and hence indication of surgery were laid down, which included:

a) Persistence of mass in the same site or fixity of the mass for more than 24 hours.
b) Persistent abdominal pain and tenderness.
c) Rising pulse rate in the absence of any mass.
d) Toxemia out of proportion to the severity of obstruction.

It was concluded that by using these criteria for indication of surgery in ascaridial obstruction significant decrease in mortality and morbidity can be achieved, in such patients.

Khurshid A Sheikh et al (1998) ; reported round worms as the most common cause of intestinal obstruction in children of Kashmir. He presented a study of 81 cases of intestinal obstruction due to round worms over a period of 2 years. 55 cases were managed conservatively and 26 including 5 cases initially managed conservatively, were taken for surgical intervention as per Dayalan criteria. Mass deworming was suggested.

Worm obstruction is the most common cause of small gut obstruction in the paediatric population in this part of the world. Most of these patients are from rural areas with lack of health education, poor hygiene and sanitation, poverty and low standard of living. Majority of the patients with worm obstruction can be managed conservatively and patients should be operated as per Dayalan criteria. As worm obstruction inflicts lot of morbidity, it is mandatory that proper health education via mass media, regarding personal hygiene, route of entry of the parasite and periodic deworming of the children is imparted, so as to reduce the incidence of this problem in our society. Further also it accounts for a large number of hospital admissions in our institution and the consequent high economic burden on the state, therefore again it is important to start the health education regarding prevention of this infection right from the admission of such patients, as this is the best time when, they and their relatives are very much receptive to the health advise.

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Personnel monitoring at Sher-i-Kashmir Institute of Medical Sciences—twenty years experience.

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Abstract

In the present investigation, an attempt has been made to study the radiation exposure of the occupational as well as non-occupational workers at Sher-i-Kashmir Institute of Medical Sciences (SKIMS), Soura, Srinagar. The radiation safety group of radiological physics and bio-engineering department is facilitated with a well equipped radiation safety laboratory. This group is assigned the job of personal and area monitoring since 1982. Every radiation worker is provided with regular TLD's for chest/wrists.

Analyzing the data on 130 occupational and non-occupational personnel, working in seven departments utilizing ionizing radiation for diagnosis and treatment (cardiology, gastroenterology, immunology, nuclear medicine, radiological physics and bio-engineering, radiotherapy and radiodiagnosis), the average cumulative lifetime dose received by workers has been determined. The maximum average cumulative lifetime dose received by a worker has been reported in the department of nuclear medicine (~17.193 msv), which is well within the permissible limit. This is followed by the department of radiodiagnosis where the dose received is 9.837 msv. In the remaining departments, most of the workers (~95%) receive the average cumulative lifetime less than 8 msv. The maximum average annual dose received by the doctors and technical persons have been analyzed separately. The maximum average annual dose received by a doctor is 1.06 msv in the department of nuclear medicine. The maximum average annual dose received by a technical worker is 1.89 msv in the nuclear medicine department, which is well below the permissible limit. Constant monitoring, education of the workers and strict adherence to the radiation protection rules and safety measures have yielded the above results.

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Introduction

The main motivation behind the study of radiation exposure of the occupational and non-occupational workers is to maintain an environment both at work as well as in the outside world where the level of radiation is relatively safe for the human beings. To achieve this goal of radiation protection, the International Commission on Radiation Protection (ICRP) has suggested that the radiation dose to an individual must be kept as low as achievable[1,2].

At present, a huge number of X-ray machines are already at work and every year a good number is added in the market for use. Besides, the radiation employing centers also get increased. The number of radiation workers also keeps on increasing with the increasing number of facilities. It has therefore, become very essential to have a centralized radiation laboratory at all these centers to take care of radiation hazards, evolution of radiation doses to both the workers and public and the measures to control the radiation leakages/unnecessary radiation exposures[3]. Evaluation of radiation dose received by the workers is referred to as personal monitoring and it plays an essential role in the protection of occupational radiation workers. It measures the quantity of radiation to which a worker is exposed through the use of thermo-luminescent dosimeter (TLD)/film badge. The TLD is one of the common devices used to estimate the level of radiation exposure to a worker.

At Sher-I-Kashmir Institute of Medical Sciences (SKIMS), Soura, Srinagar, which is a 600 bedded hospital[4], only one of its kind in the state of Jammu and Kashmir, the ionizing radiation sources include X-ray plants, sealed and unsealed radioisotopes used for diagnosis, treatment and research. These departments are cardiology, gastroenterology, immunology, nuclear medicine, radiological physics and bio-engineering, radiotherapy and radiodiagnosis. In all these departments, the personal monitoring is based on the program, which was established in its present form in 1982[5]. Extreme care is being taken to ensure radiation safety standards in all the above mentioned departments.

Keywords : Personnel Monotoring, Radiation, dosermo-luminescent dosimeter (TLD)

The radiological safety group of radiological physics and bio-engineering is facilitated with a well equipped radiation safety laboratory. This group is assigned the job of personal and area monitoring to ensure the radiation safety and protection at SKIMS. The concept of Time, Distance and Shielding help in attenuation and minimization of levels of radiations, thus bringing very close to the principle of ALARA[4].

In this study, the data on 130 personnel working in the above mentioned departments has been analyzed. The results on average cumulative lifetime and the maximum average annual dose received by the workers during the last twenty years in different departments of the institute are presented.

Material and Methods

The radiation safety group of the radiological physics and bio-engineering department is facilitated with a well equipped radiation safety laboratory. This group is assigned the job of personal and area monitoring to ensure the radiation safety at SKIMS. Every radiation worker is registered with the radiation safety laboratory for routine monitoring. Every worker is facilitated with thermo-luminescent dosimeters (TLD) for wrists and chest with his identity number written on it. The TLD, film badge and pocket dosimeters are used all over the world for the measurement of radiation exposure to the radiation workers.

All the workers wear TLD at proper places during their work in the radiation prone areas of the institute. After every three months, the TLD's are returned to the radiation safety laboratory and fresh ones are obtained. Special boxes are used to keep these TLD's safe from any misuse or overuse. These TLD's were sent to Bhabha Atomic research Centre Mumbai (BARC) for analysis and results. Now these TLD's are being sent to the Renentech Laboratories Private Limited on the recommendations of BARC. The radiation safety laboratory keeps a record of the radiation exposure of an individually monitored person integrated over a calendar year and over the entire period of his stay at the institute for further statistical evaluation.

Results and Discussion

As permitted by ICRP[5,6] the effective dose limit for uniform whole body exposure for occupational as well as non-occupational workers during the five year block is 100 msv, which means 20 msv per year on an average, with an additional condition that the dose in any single year should not exceed 50 msv. However, the Atomic Energy Regularity Board (AERB), Government of India on the recommendations of ICRP has set a dose limit of 30 msv in any one year.

To see if the radiation doses received by the workers at our institute fall within the permissible limit, we plot in Fig. 1 the average cumulative lifetime dose received by a worker in various departments. From the figure, it can be observed that the maximum average cumulative lifetime dose is received in the department of nuclear medicine, which is 17.193 msv. This is what is to be expected as the handling of open sources in nuclear medicine department adds more and more to the overall and average values of radiation exposures. The second highest average cumulative lifetime dose received is in the radiodiagnosis department, where the observed dose is 9.837 msv. In the remaining departments, most of the workers about 95 percent receive the average cumulative lifetime dose less than 8 msv. It may be pointed out here that in the departments of radiodiagnosis and gastroenterology, the trend of radiation dose received by the workers during the last few years has increased. This is due to the use of C-arm in these departments.

In Figs. 2-8, we plot the average annual dose of each worker in the above departments in order to investigate the annual radiation exposure of the workers. From these figures, it can be seen that in all the departments, the average annual dose for individual workers is well below the permissible dose recommended by International Commission on Radiation Protection (ICRP)[7]. In the department of cardiology, the maximum radiation dose received by a worker is 0.82 msv. Similarly, in the departments of gastroenterology, immunology, nuclear medicine, radiological physics and bio-engineering, radiotherapy and radiodiagnosis, the maximum average annual dose received by any worker are 1.56, 0.49, 1.89,

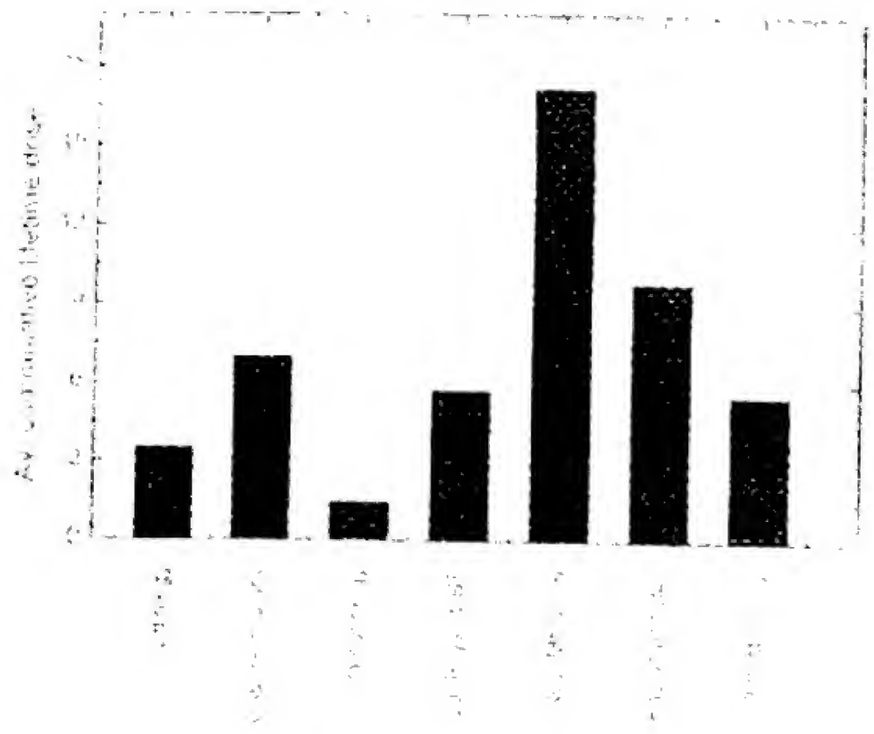


Fig. 1 Plots of average cumulative lifetime dose received by radiation worker in the seven radiation using departments at SKIMS

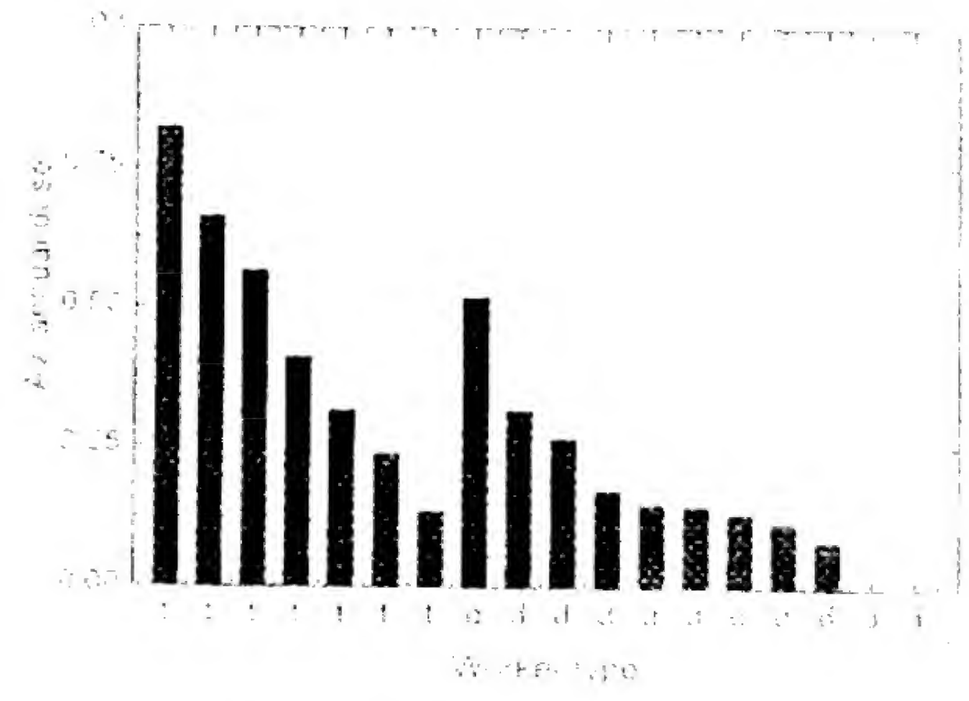


Fig. 2 Plots of average annual dose received by the radiation worker in department of radiology [illegible]

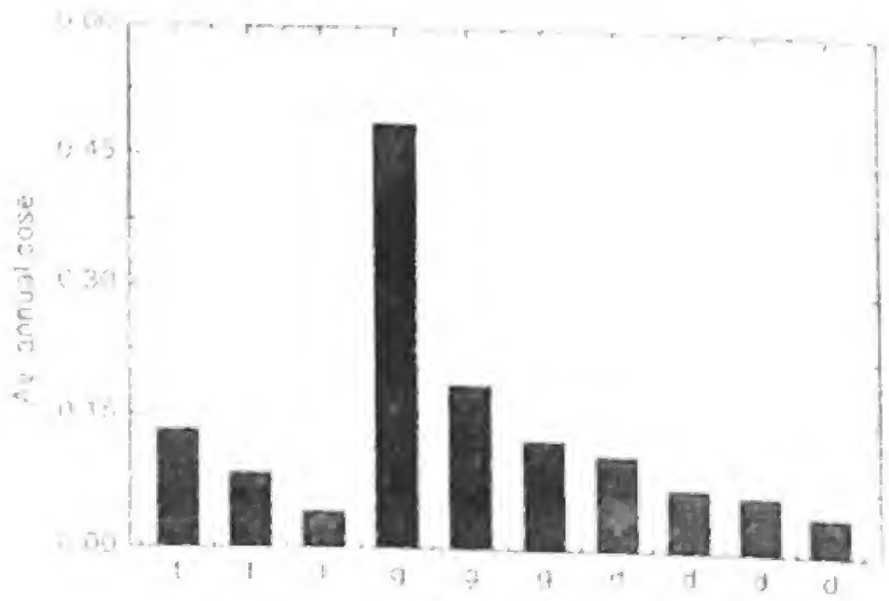
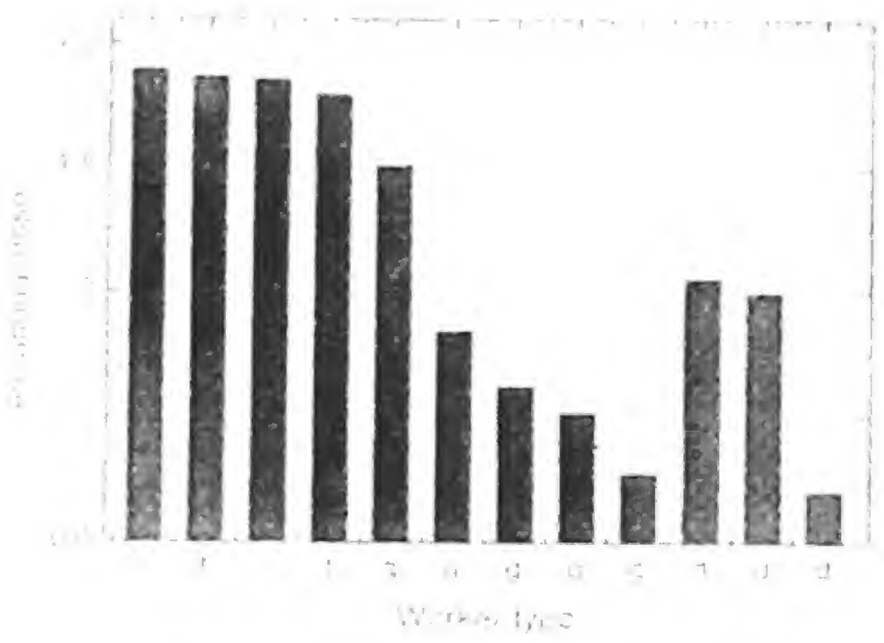
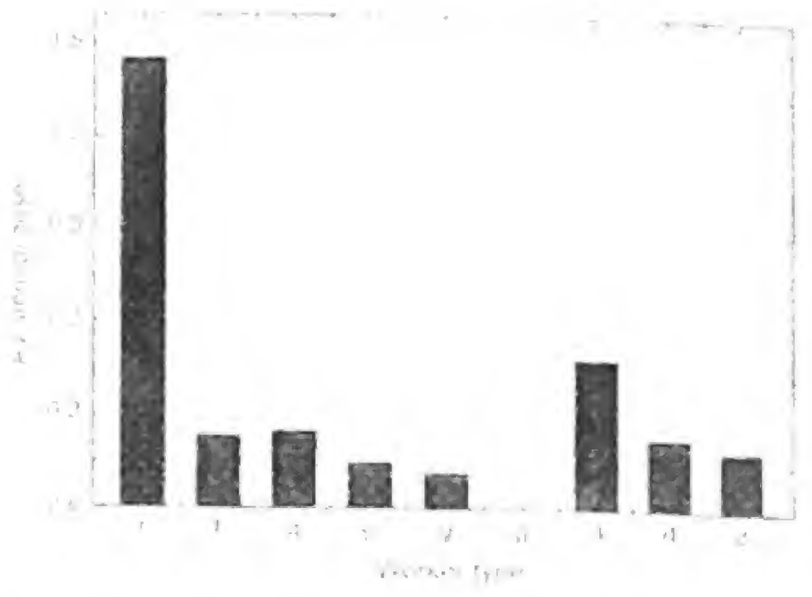
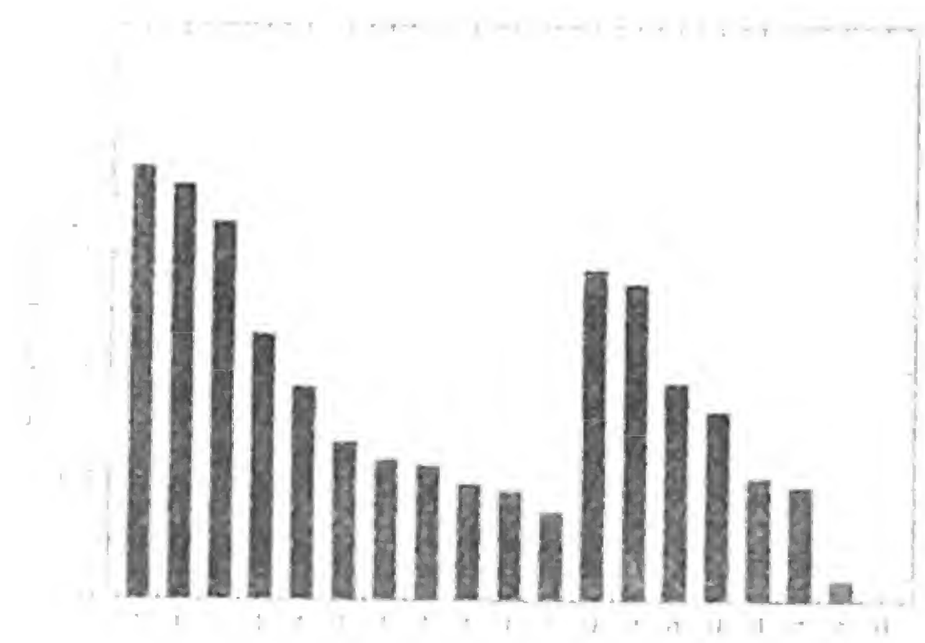


Fig. 4 Plot of average annual dose received by the individual workers in the department of immunology. t = technical person, d = doctor, o = others







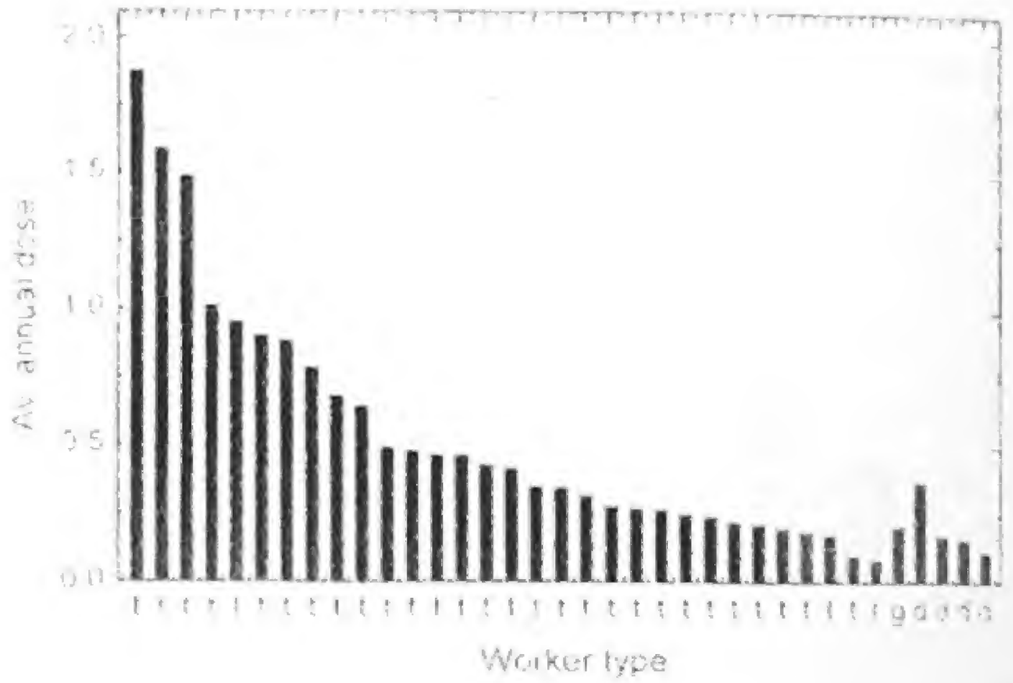


Table 1. Maximum average annual dose received by a doctor and a technical person in seven radiation using departments at SKIMS.

DOCTOR			TECHNICAL PERSON		
Worker ID No.	Department	Average Annual Dose (msv)	Worker ID No.	Department	Average Annual Dose (msv)
362	Cardiology	0.32	322	Cardiology	0.82
340	Gastroentrology	0.83	151	Gastroentrology	1.56
02	Immunology	0.11	376	Immunology	0.13
94	RP & BE	0.49	104	RP & BE	1.46
271	**Nuclear Medicine**	**1.06**	**48**	**Nuclear Medicine**	**1.89**
358	Radiodiagnosis	0.37	24	Radiodiagnosis	1.87
344	Radiotherapy	0.58	225	Radiodiagnosis	0.75

1.45, 0.75 and 1.87 msv respectively. From Fig. 5, it can be seen that the average annual doses received by the technologists in the department of nuclear medicine are relatively higher but within the permissible limit than the other workers of the department. This is because they are working with the open sources during the processes of separation, solvent extraction, purification and patient work in a radioisotope hot laboratory of the department. This needs a special attention and care.

Fig. 6 shows that one worker from radiological physics and bio-engineering has received higher dose than the other workers. On analysis it was found that the concerned radiation worker has served in the department of nuclear medicine for a long period of his service. Further from Fig. 8, it can be observed that a few workers from radiodiagnosis department are not showing compliance with their colleagues. This is attributed to their fluoroscopic work in the department.

Table 1 presents the maximum average annual radiation dose received by the doctors and technical persons from the seven ionizing radiation using departments. From the table, it can be seen that the maximum average annual dose received by a doctor is in the department of nuclear medicine, which is 1.06 msv. Further, the maximum average annual dose received by a technical worker is 1.89 msv and the worker again belongs to the department of nuclear medicine, however, in both the cases the received dose is less than 2 msv, which is well below the permissible limit. It is worthwhile to mention here that the study makes a point for authorities to become cautious for the workers of nuclear medicine department. Although the doses received by individual workers in this department are well below the allowed limit, yet needs a special care to further strengthen the principle of As Low As Reasonably Achievable.

Conclusions

From our systematic study of radiation exposure to the radiation workers working in various departments of the institute using ionizing radiation for diagnosis and treatment, it is observed that all the radiation workers have received the radiation dose well below the permissible limits, thereby indicating good protective measures taken by the institute authorities viz design and construction of the ionizing radiation facilities in collaboration with AERB and following the radiation protection rules of Government of India strictly.

Further properly trained radiation workers and constant monitoring by the centralized radiation safety laboratory with all the facilities for area surveys, radiation emergencies and personnel monitoring helps in maintaining the highest safety standards.

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original article

Profile of Liver Trauma

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Abstract

The aim of this study was to understand the profile of liver trauma in Kashmir which was struck with violence recently and the influx of liver trauma patients also increased. A prospective as well as a retrospective study was conducted on 200 patients of liver trauma at Sher-i-Kashmir Institute of Medical Sciences which is a tertiary care hospital of the valley. Total of 200 patients were analysed. Age ranged from 1 year to above 50 years. Mean age was 24.25±12.84, males: 179, females: 21, M:F=8.5:1, blunt trauma: 45%, penetrating injuries: 55%. Right lobe was the commonest site (76%), revised trauma score (RTS) ranged from 1.15-7.84 with mean RTS of 5.61, injury severity score (ISS) ranged from 11-50, mean: 29.04±10.47. 41.5% of patients had grade IV, 35% grade III, 12% grade II and 11.5% grade I injuries. Commonest associated intra-abdominal injury was small gut (44.5%), followed by colon (31.0%). 64% of patients underwent hepatorrhaphy. Lobectomy/ segmentectomy was done only in 3% of cases. Overall complication rate was 34.5%. Overall mortality was 42% and hepatic mortality 23.5% only. Lobectomy /segmentectomy had 50% mortality, whereas hepatorrhaphy had only 16% mortality. 80% survival was seen in patients with RTS of 6.53-7.84 with p-value of <0.001. 95% survival was seen in patients with ISS of 11-15 (p-value of <0.001). Grade IV trauma had 38.55% mortality whereas grade I had 0% mortality (p-value 0.004). It is concluded that liver injury is a serious, complex and difficult injury to deal with. Cause of death is multifactorial. Complication rates are also high. Early effective resuscitation with fluids and blood as well as proper application of surgical options and effective postoperative care can further improve the outcome.

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INTRODUCTION

Liver injury is the second leading cause of death due to blunt trauma and commonest organ to get injured in penetrating injuries. It is the leading cause of death among people of 1-36 years.[1] Liver injuries can be isolated but is usually associated with injuries to other organs. Among liver injuries, injuries to the portahepatis, hepatic veins and retro-hepatic venacava are less common but most difficult to manage in non- specialised centres. It is the liver parenchymal injury, which is more commonly encountered.[2]

Based on World War II experience Madding and Kennedy recommended liver resection as the primary treatment of major liver trauma. They also noted highest mortality in combined injuries of liver and colon getting injured simultaneously. During the next few years the management of liver injuries continued to evolve and certain modalities like hepatic labectomies, intra hepatic packings, deep mattress sutures and hepatic artery ligations were discouraged due to mortality of more than 50%. Hepatorrhaphy and debridement was found to have more survivability though complications were high. Therefore packing was reintroduced in 1980's.[1]

Experience with hepatic injuries provided by the military surgery continued in the later wars. The 27% mortality in World War II reduced to 14% in Korean War and 8.5% in Vietnam War .[1,4]

More recently, two significant events have changed the approach to hepatic trauma. They are: a) Understanding of segmental anatomy of liver, which enabled selective hepatic resections and b) Liver transplant operations.

Nowadays seven basic techniques are used in the operative management of liver injuries: 1) Suture, 2) Inflow occlusion 3) Packing, 4.Hepatic artery ligation, 5)Resection, 6) Mesh hepatorrhaphy and 7) Atrial caval shunting.

MATERIAL AND METHODS

The study was conducted from December 1982 to December 1998 (retrospective study) and January 1999 to Dec. 2000 (prospective). There

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Key words: Liver trauma, lobectomy, packing, hepatorrhaphy

were 160 patients in retrospective and 40 in prospective study. Study was conducted in the department of General Surgery at SKIMS Soura, Srinagar.

All the patients were admitted in accident and emergency department of SKIMS with abdominal trauma or polytrauma. Relevant brief history and examination findings were recorded, patients resuscitated as per the need. All base line investigations like haemogram, Bl.glucose, KFT, electrolytes, blood grouping and other relevant investigations like USG abdomen and DPL/Four quadrant aspiration were done as per the need and protocol. Tetanus prophylaxis was given to all patients. Patients who were haemodynamically stable, were monitored strictly and any change in haemodynamics were attended to as per need. The following parameters were recorded in all patients at the time of admission: 1) Level of consciousness, 2) Breathing, 3)Pulse and blood pressure, 4) Glasgow coma score, 5) Abdominal signs, 6) Associated injuries, 7) Paracentesis /DPL (+ or -), 8) Assessment of revised trauma score (RTS) and 9)Assessment of injury severity score (ISS).

Patients with penetrating injuries or with shock were immediately taken to operation theatre for exploratory laparotomy after resuscitation. All other patients were observed and monitored strictly for vitals and further investigations were ordered. They were subjected to surgery only if their investigations or physical findings suggested so. Laparotomy was carried out through a midline incision. At Laparotomy, site and extent of injuries were noted. Liver injuries were graded according to Moore et al.[4] Other intra abdominal injuries were also noted. Immediate attention was given towards the arrest of bleeding and making the patient stable. Then the liver injuries were dealt with according to the severity of injury, by different methods like hepatorrhaphy, temporary packing, Pringle's manoeuvre, segmentectomy, lobectomy, hepatic artery ligation etc. However in emergency our primary aim was to control bleeding and make the patient stable by the minimum possible intervention. Other associated intra-abdominal injuries were also dealt with accordingly.

Due attention was also given to the other associated extraabdominal injuries. After surgery patients were shifted to postoperative ward or SICU. Patients were managed on I/V fluids, antibiotics and analgesics. Investigations like haemogram, KFT, blood glucose, electrolytes, coagulogram, LFT and USG abdomen were carried out regularly till the patients recovered fully. In all patients revised-trauma score and injury severity score were also noted down for analysis.

In the retrospective group also the above parameters were noted from the records. Patients with incomplete records were excluded from the study. Follow up was complete approximately in 82% of the patients for a period of3-6 months.

RESULT

The study being a retrospective as well as prospective study, a total of 200 patients were included in the study; retrospective 160 and prospective 40 patients. Most of the patients were in the age group of 11-40 yrs. with mean age of 24.25±12.84, median age of 24.21. Extremes of ages found be to spared. Maximum patients were Males 89.5% M: F ratio of 8.5:1. Mode of injury consisted of blunt trauma 90/200(45%); gun shot injuries 60/200 (30%), blast injury 45/200 (22.5%) and stab injuries 05/200 (2.5%). Gunshot and blast injuries constituted the majority i.e. (75 %). Blunt trauma was the common mode of injury during the peace time. Clinical presentation of patients is shown in Table 1.

The right lobe was the commonest site of injury (76%), followed by left lobe was seen in 20% and portahepatis in 4% of cases. Hepatic vein and vena caval injuries were not seen in any. Revised trauma score ranged from 1.15-7.84 as shown in Table 2. Median range was 6.03 & Mean range 5.61. Distributions of patients as per the grade of injury is shown in Table 3. Most of the patient 60 (30%) were in the Injury Severity Score (ISS) range of 46-50. Highest ISS obtained was 50, where as lowest was 11. Mean±SD was 29.94±10.47 and median 30.26 (Table 4).

Out of the 200 patients, 44.5% had associated small bowel injury, 31% had colon injury and 13% had stomach injury. Other associated injuries were; retro peritoneal heamatoma-9%, spleen 8.5%, duodenum 4.0%, kidney 3.5%, panereas 2.5% biliary tract 2.5%, uterus 1.5% and urinary bladder in 1.5%.42 patients had more than three associated organ injury. Twenty one patients had isolated liver injury, out of which one developed biliary fistula which was managed conservatively. Table 5 represents the number of patients treated by different modes of management. Main complications encountered in patients of liver trauma were deranged liver function (16.5%), coagulopathy (18%), respiratory complication (27%) wound dehiscence (7%) and intra-abdominal complication (21.5%). The overall mortality was about 42%. Whereas mortality related to liver injury only was 23.5%; 18.5% of patients died of other causes (Table 3). Commonest cause of death was irreversible shock due to blood loss; 36/84 (43%), Septicemia 13/84 (15%), severe head injury 09/84 (11%), ARDS 02/84 (2%), coagulopathy 15/84(18%), renal failure 02/84 (2%) and hepatic failure 07/84 (8%).

When the number of deaths were compared as per the mode of management, Hepatorrhaphy had only 21/128 (16%) deaths as compared to labectomy/ segmentectomies 3/6(50%), packing only 11/30 (37%), Hepatic artery ligation (33%), repair and packing (28%), selective hepatic artery ligation (20%) and omentoplasty 17% (Table 5).

Revised trauma score (RTS) was found directly proportional to survival with p value of <0.001 - Table 2. Similarly ISS was also proved to be a good predictor of survivability with Survival ISS =25.45± 8.54. Expiry ISS =37 (81± 8.15) t =10.2453, p = <0.001 (Table 2 and Figure 1).

Last but not the least, mortality was very significantly related to the Grade of liver injury. Higher the grade, higher the mortality (Table 3). The number as well as the site of associated injuries had direct relation with mortality, especially associated colonic injuries which increased mortality sharply.

DISCUSSION

Hepatic injuries remained a subject of interest and challenge to the surgeons because of the ever increasing violence & accidents worldwide as well as the complexity of the management of liver trauma.

We conducted the study in our hospital because the

Table 1

Distribution of patients according to clinical presentation

Sympton/sign	No. of patients	Percentage	
Haemoperitoneum	170	85	
Pain abdomen		162	81
Penetrating wound		125	62
Poly trauma	90	45	
Shock	80	40	
Haemothorax	20	10	

Table 2

Distribution of patient according to RTS score and survival/mortality (n=200)

RTS	Number (%) of patients	Number (%) of patients died	Number (%)of patients survived
1.15-2.49	15 (100)	13 (87)	2 (13)
2.5-3.83	29 (100)	22 (76)	7 (24)
3.84-5.18	34 (100)	18 (53)	16 (47)
5.19-6.52	27 (100)	10 (37)	17 (63)
6.53-7.84	95 (100)	21 (22)	74 (80)
Total	200 (100)	84 (42)	116 (58.0)

p = <0.001

Table 3

Distribution as per the grade of liver injury and related mortality

Grade of injury	Number (%) of patients	Overall mortality (%)	Hepatic mortality (%)
I	23 (11.5)	4 (17)	0 (0)
II	24 (12.0)	5 (21)	2 (8)
III	70 (35.0)	34 (49)	13 (19)
IV	83 (41.5)	41 (50)	32 (39)
V	-	-	-
VI	-	-	-
Total	200 (100)	84 (42)	47 (23.5)

p = 0.004 (significant)

Table 4

Distribution and survival in relation to injury severity score (ISS)

ISS	Total number of patients	Patients survived	Percentage
11-15	20	19	95
16-20	21	19	90
21-25	29	23	79
26-30	32	22	69
31-35	22	13	59
36-40	7	3	43
41-45	9	3	33
46-50	60	14	23
Total	200	116	58.00

Survival ISS=25.45±8.54,
t=10.2453,
Mean distribution ± SD = 29.04± 10

Expiry ISS=37.81±8.15,
p=<0.001 highly significant
Median distribution =30.26

Table 5

Comparison of mortality as per the type of repair

Type of repair	Total number of cases(%)	Number of deaths (hepatic)	Percentage of deaths
Hepatorrhaphy	128 (64)	21	16
Packing only	30 (15)	11	37
Repair and packing	18 (9)	5	28
Selective hepatic artery ligation	6 (3)	1	20
Omentoplasty	6 (3)	1	17
Hepatic artery ligation	3 (1.5)	1	33
Lobectomy/segmentectomy	6 (3)	3	50
Total	200	47	23.50

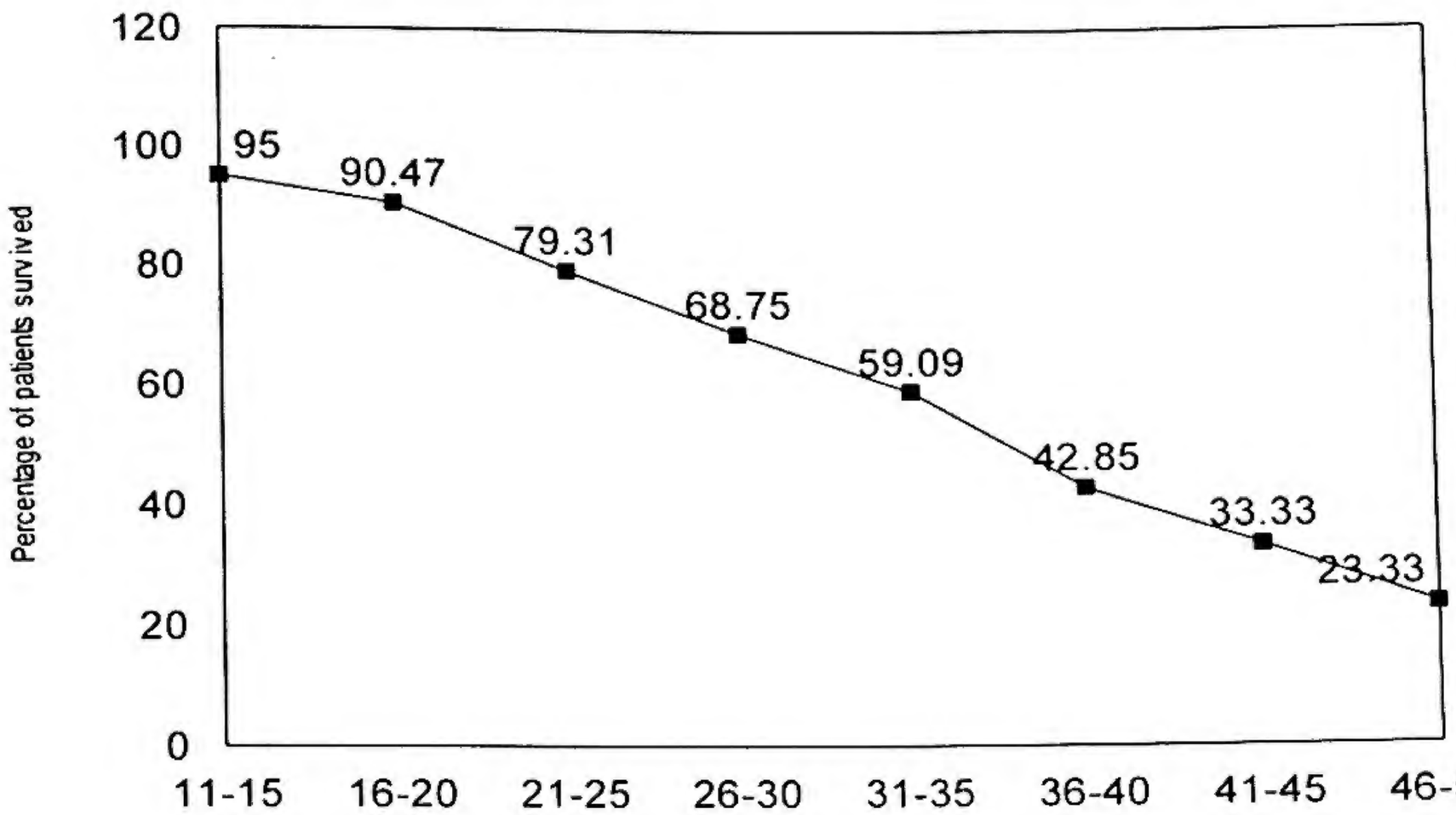

Figure 1: Survival of patients in relation to ISS

incidence of liver injuries grew sharply in this part of the world during the past one-decade or so. The surgeons felt the need to update the management policies viz a viz-liver injuries.

Out of 200 patients of our study, about 149(74.5%) patients were in the age group of 11-40yrs. with mean age of 24.25±12.84. The age distribution in our study was comparable with other studies.[6-11]

Extremes of ages are spared possibly because of sedentary life style. Males (89.5%) out numbered the females 10.5%. Male to female ratio of 8.5:1. This is similar to the study conducted earlier.[12] The ratio has been less in other studies.[6,13] Higher M: F ratio in our study is explained by the fact that majority of the females remain indoors.

The commonest mode of injury in our study was missile injuries (52.5%, Gunshot +Blast) compared to blunt trauma (45%). Stab injuries consisted only 2.5%.

Similar results are reported in other studies as well[7,11,12,14] except for the stab injuries which is explained by the fact that, stabing in not known in Kashmir. The incidence of penetrating injuries has also gone up because of the prevailing violence in the valley. 85% of patients presented with frank hameoperitoneum followed by pain abdomen 81% and visible penetrating wound in 62.5% of cases (Table 1). Commonest site of injury was right lobe – 76% followed by left lobe 20%. Portahepatis – 4%. In two patients more than two sites were injured. Similar findings were observed by W. Peter Geis et al.[15]

Revised trauma score (RTS) was found to be a good predictor of survivability and prognosis (Table 2) with *p* value of <0.001. Mean RTS was 5.61. Median 6.03. Similar observations were also shown in earlier studies.[10] Injury severity score (ISS) was again a good prognostic indicator inversely proportional to survivability. Mean ISS was 29.04±10.47 and medium = 30.26. Survival ISS=25.45±8.54 expiry ISS=37.81±8.15, t = 10.2453, *p*

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Laparoscopic cholecystectomy experience in the rural health sector of Kashmir

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Abstract

This study was conducted in the department of Surgery, District Hospital Baramulla, Kashmir on 100 consecutive patients who presented with symptomatic gall stones from June 2004 till December 2005. There was no selection criteria and all patients irrespective of their age, sex, past history of acute cholecystitis, obesity and previous lower abdominal surgery (LSCS, hysterectomy etc.) were subjected to laparoscopic cholecystectomy. However, patients with associated pathology like choledocholithiasis, gall bladder malignancy, uncorrectable coagulopathy and severe cardiopulmonary disease were not included in the study. Mean age of the patients was 40.03±9.9 years (range 18-70). Male to female ratio was 1:3.7. The procedure was performed successfully in 90 cases (90%). In 10 cases (10%), a conversion to standard open cholecystectomy was necessary, the most common cause being unclear anatomy. There was no major complication in our series but few minor complications. The mean operative time was 96.9 minutes (range 45-250 minutes). The mean hospital stay was 1.8 days ± 0.46 SD (range 1- 3 days). No death occurred in our series. Our results suggest that laparoscopic cholecystectomy can be safely adopted as a gold standard for the treatment of gall stones and major benefits to the patient are short hospital stay, decrease postoperative pain, better cosmesis and early return to work.

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Gall bladder disease continues to be one of the most common digestive disorder encountered by physicians[1]. Cholelithiasis affects an estimated 15 to 20 million people in the United States, with more than 500,000 cholecystectomies performed each year[2]. This disease is also very common in our part of the country[3]. Laparoscopic cholecystectomy (LC), performed for the first in 1987 by Movret in France is now Gold Standard for the treatment of symptomatic gall stones[4,5]. LC has the advantages of minimal wound pain, short hospital stay, good cosmesis and early return to work[6]. This procedure was first launched in our hospital on 7th June 2004, making us the first Rural District Hospital of the department of Health Services, Jammu and Kashmir to adopt laparoscopic cholecystectomy as the Gold Standard for treating symptomatic gall stones. We report here our results during the first year of laparoscopic cholecystectomy in our hospital.

MATERIAL AND METHODS

From June 2004 till December 2005, 100 patients (21 males and 79 females) with symptomatic gall stones underwent laparoscopic cholecystectomy. Diagnosis of gall stones was confirmed by preoperative ultrasonography in all the patients. Detailed history was taken and thorough examination conducted in all the patients prior to surgery. The procedure and the risk of conversion of open were fully explained to patients and written consent was taken for the said procedure in all the patients. Routine preoperative investigations (full blood count, clotting profile, liver function tests, kidney function tests, blood sugar, serum electrolytes) were performed in all the patients. Patients were asked to remain fasting on the day of surgery and all patients were operated under general anaesthesia. No urinary catheter was inserted but the patients were asked to void first before entering the operation theatre. A nasogastric tube was inserted shortly after the induction of general anaesthesia and removed at the end of the procedure. All patients received a single intravenous dose of prophylactic antibiotic (Ceftriaxone 1 gm) with the induction. The operative procedure was conducted in the manner described by others[7,8]. Tube drain was kept in all the patients. Postoperatively, the patients were allowed oral fluids once fully recovered from the anaesthesia. Most of the patients were discharged on the second postoperative day. The patients were advised to come for follow up in the outpatient clinic.

Key words: *Gall stones, Laproscopic Cholecystectomy, Rural health*

Table 1: Demographic data of patients

Total number of patients	100
Males	21
Females	79
Female : Male ratio	3.7 : 1
Mean age of patients ±SD	40.03 ± 9.9 years
Range	18-70 years
Mean age of females ± SD	46.7±4.2
Range	18 - 66
Mean age of males ± SD	37±12.5

Table II: Operative findings

Operative findings	No. of patients	Percentage
No adhesions or flimsy adhesions	72	72
Dense adhesions (omental), easy to separate	18	18
Dense omental adhesions, difficult to separate	7	7
Adhesions with duodenum and colon	3	3
Thin walled gall bladder	79	79
Thick walled gall bladder	14	14
Mucocoele of gall bladder	6	6
Empyema with gangrenous gall bladder	1	1
Accessory cholecysto hepatic duct	1	1

Table III: Reasons for conversion

Reason	No. of patients	Percentage
Frozen Calot's and unclear anatomy	6	6
Dilated CBD with choledocholithiasis	2	2
Hemangioma liver near Calot's	1	1
Mirrizi I syndrome	1	1

Table IV: Distribution of cases according to complications

Complications		No. of patients	Percentage
A)	**Intraoperative**		
	Perforation of gall bladder with spillage of bile	17	17
	Perforation of gall bladder with spillage of stones & bile	6	6
	Bleeding from liver bed controlled with diathermy	8	8
	Bleeding from liver bed controlled with surgicel	1	1
	Bleeding from cystic artery	3	3
	Subcutaneous emphysema	1	1
	Bleeding from umbilical port	1	1
B)	**Post operative**		
	Port site infection	2	2
	Persistent drainage	1	1
	Ileus	1	1

RESULTS

In this series of 100 patients, mean age of the patients was 40.03 years (range 18-70). Female to male ratio was 3.7:1. The demographic data are shown in Table I. All patients were admitted for elective cholecystectomy. The mean operative time i.e., time from making an incision for insertion of veress needle to the time of applying dressing was 96.9 minutes (range 45-250 minutes). The operative findings are listed in Table 2. The procedure was converted to open cholecystectomy in 10 patients (10%) and the reasons for conversion are listed in Table 3. The mean hospital stay was 1.8 days ± 0.46 SD. The mean hospital stay for converted cases was 4.1 days ±0.02 SD. None of the patients had major complications. Minor complications were divided into intraoperative and postoperative complications. The various complications seen in our series are listed in Table 4.

DISCUSSION

Since the introduction in Lyon, France by Movret in 1987[9], laparoscopic cholecystectomy is now Gold Standard for the treatment of symptomatic gall stones[4,5,10]. It is now offered to all corners with a success rate of 99%[11]. Our mean operative time was 96.9 minutes which is well within the range reported by others[7,11]. It is well known that the operative

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Abstract Abstract Abstract

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4) Written consent

Exclusion criteria:

1) Intraventricular hemorrhage
2) Congenital infection
3) Sterile cultures

Clinical Signs of sepsis were defined by the presence of at least two of the following:-Feeding intolerance, abdominal distension, lethargy, irritability, temperature instability, hyperbilirubinemia and hepatosplenomegaly. All neonates with abdominal distention had an x-ray examination at the outset. There was no evidence of NEC at that stage of infection according to Bells staging. Respiratory dysfunction was diagnosed by presence of tachypnoea (>70 breaths/min) or episodes of apnoea (> 20 sec). Circulatory dysfunction was determined by presence of tachycardia (Heart rate > 190 beats/min), Bradycardia (heart rate < 90 beats/min), prolonged capillary filling time (>2sec), mean arterial blood pressure less than 30 mmHg and increase in fraction of inspired oxygen (FiO2). Shock was defined by presence of a mean arterial pressure <20 mmHg with sudden deterioration clinical status (apnoea, Fio2 > 0.8, pallor, anuria, metabolic acidosis), requiring higher dopamine (> 5 microgram/kg/min) or volume infusion [10]. Samples for blood culture were obtained from both groups on day one. Blood samples were sent for CBC, platelet count, plasma protein level, ABG, KFT, CRP, Micro ESR, Electrolytes, Sugar, Calcium. CSF and urine examination was done. Cranial USG was done to rule out intra cranial bleed. X-ray chest and abdomen was done as routine.

Neonates were divided into two groups: Group I (study group) were assigned to receive Pentoxifylline in addition routine therapy of sepsis. Group II (control group) only received routine therapy of sepsis. The PTXF was given intravenously in a dose of 5 mg/kg/hr for 6 hours. The infusion was repeated on 2nd and 3rd day of therapy. Routine medical management of sepsis in both groups was comparable. Amoxicillin + Clavulanic acid and Amikacin were first line antibiotics. After blood culture reports antibiotics were adjusted according to sensitivity of the isolated organism. Protocols for Dopamine and Dobutamine administration were identical for both groups. The criteria for artificial ventilation and for weaning from the ventilator were comparable.

FOLLOW UP:

Neonates treated with Pentoxifylline were monitored for adverse reaction i.e. hypertension, irritability, deterioration of vital signs. Systemic arterial pressure was recorded continuously during the 3-5 days period beginning at the first onset of sepsis in both groups. Arterial blood sampling was done at similar intervals of time (4-8 hours) in both groups to determine acid base balance. For WBC, platelet count and plasma protein level, blood samples were taken daily from peripheral vein. Daily urine volume was measured during first three to five days of sepsis. Renal insufficiency was defined when urine output was less than 1 ml/kg/hr.

Results:

Table - 1 Baseline Characteristics of two groups

Characteristics	PTXF Group(n=25)	Control group (n=25)
Birth weight (grams)	950-2580 (range)	1000-2650 (range)
Apgar Score	5-9 (range)	5-9(range)
Gestational Age (weeks)	32-37 (range)	32-37 (range)
Hypotension	18 (72%)	17(68%)
Symptoms of shock	10 (40%)	9(36%)
Neutropenia (<2000/mcu)	13(52%)	12(48%)
Hypoproteinemia(<5 g/lit)	6(24%)	6(24%)
Metabolic acidosis in arterial sample(ph <7.23& bicarbonate level< 17 Meq/l)	11 (44%)	12(48%)
Thrombocytopenia	21 (84%)	22 (88%)
Abdominal distention	6 (24%)	5(20%)
Need for ventilation	4 (16%)	3 (12%)

The study consisted of 50 premature infants who had culture proved sepsis. Neonates were divided into two groups: Group I (study group) were assigned to receive Pentoxifylline in addition routine therapy of sepsis. Group II (control group) only received routine therapy of sepsis.

Table 2 : Organisms causing sepsis

Organism	Survivors		Deaths	
	PTXF group n=21	*control group* n=15	*PTXF group* n=4	*control group* n=10
Escherichia coli	*3(14.3%)*	*2(13.3%)*	*1(25%)*	*2(20%)*
Klebsiella pneumonia	*12(57.!%)*	*5(33.3%)*	*2(13.3%)*	*7(70%)*
Serratia marcescens	*1(4.8%)*	*1(6.6%)*	*1(25%)*	*1(10%)*
Enterobacter cloacae	*2(9.5%)*	*1(6.6%)*	*0*	*0*
Proteus	*1(4.8%)*	*0*	*0*	*0*
Staphylococcus aureus	*2(9.5%)*	*4(26.66%)*	*0*	*0*
Staphylococcus epidermidies		*0*	*2(13.3%)*	*0* *0*

Baseline characteristics in two groups were similar (Table-I)

With no significant differences at randomization with regard to birth weight, gestational age, apgar score, occurrence of shock, hypertension, Neutropenia

hypoproteinaemia, metabolic acidosis, thrombocytopenia, abdominal distention. The causative organisms isolated from blood cultures are listed in table2

In the study group, 4 of 25 infants (16%) died due to sepsis. However, in control group 10 of 25 (40%) neonates died of sepsis. The difference in mortality is quite significant (P < .02). Considering exclusively sepsis caused by gram negative bacteria in the study group 19 of 23 (83%) neonates survived, whereas in control group only 9 of 19 (48%) neonates survived. The difference noted is again quite significant (P < .04). No mortality was observed in neonates with gram positive sepsis in both groups. Only 1 of 10 (10%) of neonates in study group with shock expired while 7 of 9 (78%) neonates with septic shock in control group expired (P < .002). In the study group 2 of 25 (8%) treated infants develop NEC during the course of sepsis while in control group 7 of 25 (28%) develop NEC. (P< .01). In the study group average duration of ventilation was 72 hours whereas in control group duration of ventilation was 120 hours which is again quite significant. In the study group duration of hospital stay was average 15 days whereas in control group duration of hospital stay was 30 days.

There was no evidence of toxicity attributable to PTXF.

Discussion:

Pentoxifylline prevents endothelial cell dysfunction in sepsis[12] preserves endothelial thrombomodulin, protein C, and the protein S anticoagulant system[13] Pentoxifylline stimulates fibronolysis associated with increase release of tissue plasminogen activator in sepsis[14] It also enhances prostacyclin release[15] attenuates the release of trhomboxane[16] Pentoxifylline does not impair platelet function[17] or increase platelet adhesion[14] Pentoxifylline increases erythrocyte and leukocyte deformability[18] and chemotaxis, decreases neutrophil degranulation and release of super oxides[19] These biological and cellular effects of Pentoxifylline have been attributed to the inhibition of both cellular phosphodiesterase and resultant increase in cyclic adenosine monophosphate concentrations. Increased plasma tumor necrosis factor alpha concentration correlates with mortality in sepsis[1] and Pentoxifylline known to inhibit TNF production may improve survival.

Results of our study showed a beneficial effect of Pentoxifylline on survival rate of sepsis of premature infants, particularly in sepsis caused by gram negative bacteria[11] Results of our study confirmed the beneficial effect of Pentoxifylline in sepsis complicated by shock. Similar results were shown by LauterbachR[1] Our study confirmed that Pentoxifylline protects against the NEC development, similar results were obtained by Lauterbach R[1] and by animal studies[21] Our study showed that duration of ventilation and hospitalization was reduced significantly. This could possibly be explained by bronchodilator and respiratory muscle stimulant effects of Pentoxifylline [22] In conclusion Pentoxifylline produces a significant reduction in all cause mortality during hospital stay in neonates with sepsis who had Pentoxifylline as an adjunct to antibiotics compared to neonates with sepsis who had not received. Pentoxifylline

A larger multicentric study is needed to determine the efficacy and safety of Pentoxifylline administration in the treatment of sepsis and co morbidities of sepsis e.g. chronic lung disease, duration of assisted ventilation, NEC, in both pre-term and term infants and to compare Pentoxifylline with other adjunctive modalities such as colony stimulating factors or intravenous immunoglobulin.

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Hairy cell leukemia with situs inversus totalis: a rare presentation

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Abstract

Hairy cell Leukemia with situs inversus is a rare presentation and not even a single case has been reported so far. For the first time such a case came to notice in the Medicine Deptt of GMC Jammu. The patient was subjected to physical exam & series of tests were carried out i.e. Lab. Tests, X-ray chest, Echocardiography etc. Chemotherapy was started after shifting the patient to radiotherapy unit and patient showed a good clinical response to treatment.

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Case Report

45 year old male, chronic smoker, non-diabetic, normotensive presented in medicine ward with history of breathlessness which was initially mild in nature and then gradually progressed to increased severity with total duration of 2 months. There was history of distension of abdomen of 2 months duration. He also had H/o fever (20 days) which was of low grade, with evening rise and associated with chills but no rigors.

Patient on general physical exam was conscious, cooperative, oriented, he had severe pallor, and pulse rate was 86/mt regular fair volume, blood pressure of 130/80 mm Hg. There was a solitary lymph node in RT Axilla (½ x ½ cm) which was freely mobile and not adherent to the overlying skin and a single café-au-lait spot seen in RT lower chest. CVS examination revealed apex beat in 4th I.C.S just 3 cm inside midclavicular line on right side. First and second heart sound were loud and marked on right side of sternum and were normal in intensity and character. No added sounds/ murmur were heard and intensity of sound was less on left side. Abdominal Examination revealed a distended abdomen with tenderness present in RHC. There was a swelling palpable 13cm below Rt. Sub-costal margin in mid clavicular line extending upto umbilicus which was firm, moving with respiration with a regular surface and a notch. There was another swelling on Lt Side which was palpable 3cm below Lt Sub costal margin. It had sharp borders had firm & regular surface. There was no shifting dullness or fluid thrill. Rest of systemic examination was normal.

Haemogram revealed anemia (4.6 gm %) which was dimorphic with few elliptoytes, Total leucocytic count was 8000/mm with polymorph 10% and lymphocytes 90%. On peripheral film there was abundance of medium sized lymphoid cells with cytoplasm showing fraying of margins and it was present in approximately 90% of cell (Picture Fig. 1).

Bone-marrow examination revealed good cellularity with moderately reduced M/E ratio and a few Megakaryocytes are seen. There was a noticeable increase of 50% in the number of lymphoid series comprising chiefly medium small sized and a few large cells over granulocyte cell series. The Cytoplasm in medium and large cells was moderately abundant agranular and few showed cytoplasmic irregularity nuclear indentation and nucleolus. However larger cells appeared as typical (blast like) hairy cell (Fig. 2).

Blood Sugar, RFT, LFT, Urine examination and S. Electrolytes were essentially normal. ECG showed: (I) Upright P wave in lead III and lead avF. (ii) Upright equiphasic P wave in lead avR (iii) Inverted P wave in lead and avL (iv) Upright QRS complex in lead III and lead av f (v) Negative QRS in lead I and avL QRS complex tallest in V I and diminished V6.

CXR (PA view) revealed; Cardiac apex pointing to the right (Detrocardia) and right sided aortic arch.USG showed Massive

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Key Words: -Situs inversus totalis, situs inversus with dextrocardia, situs inversus with levocardia, mirror image of situs solitus, situs solitus, situs ambiguous, kartagener's syndrome.

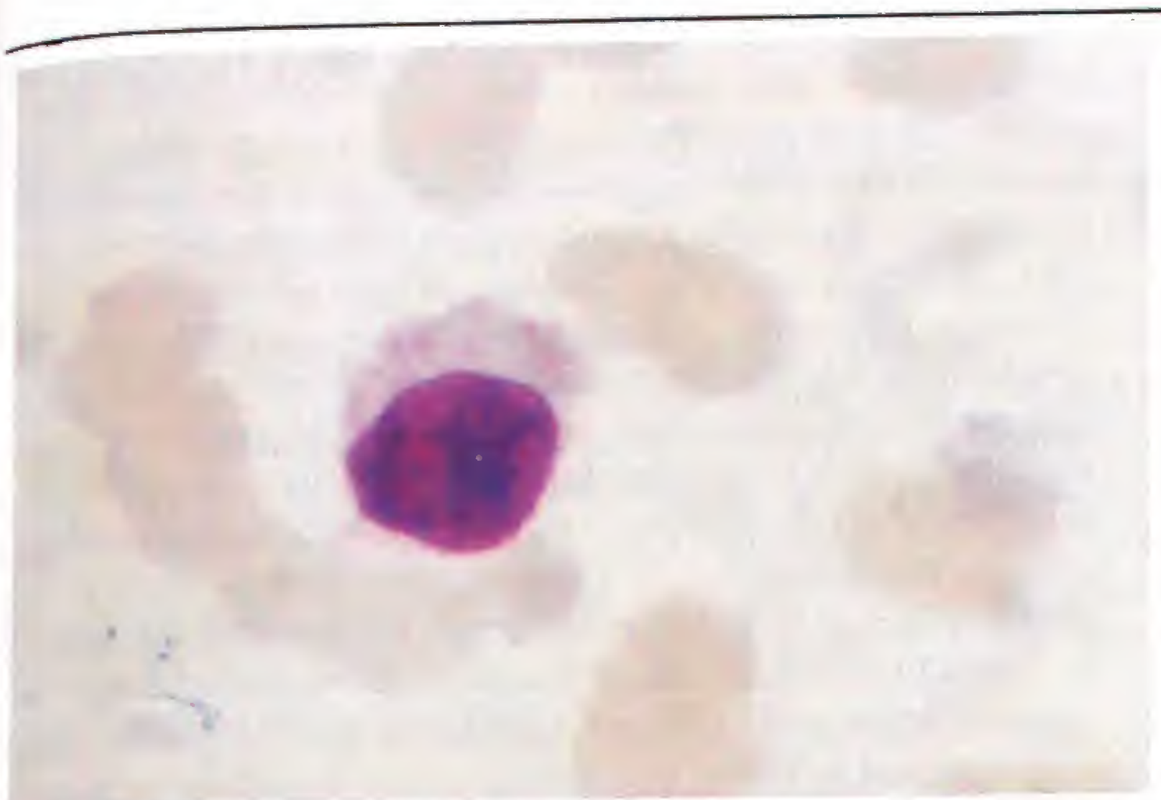

Figure 1. Photomicrographs of PBF. 100 x magnification; shows typical large cells with moderate amount of cytoplasm that has serrated margins-hairy cell projections.

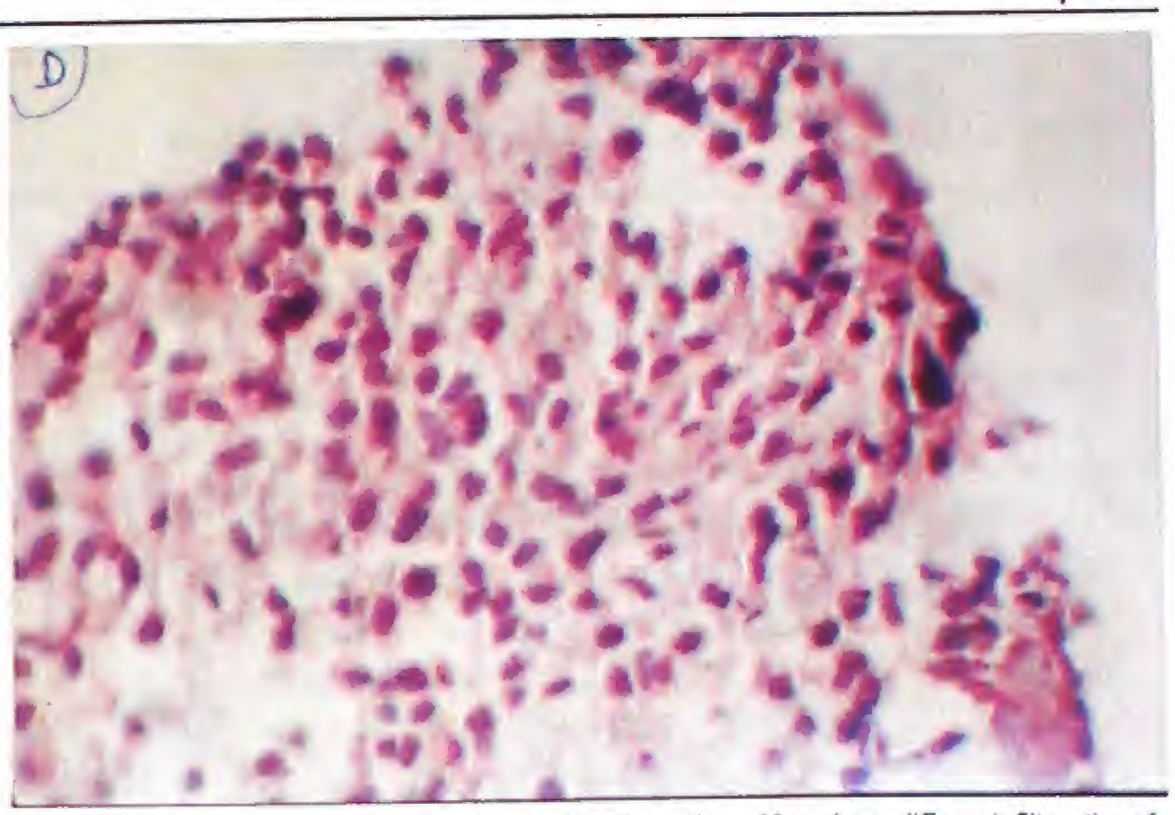

Figure 2- Bone marrow trephine biopsy (H&E) section. 40x. show diffuse infilterationof these mononuclear cells. The arrangement of cellular infiltrate is loose and show spacing of the cells.

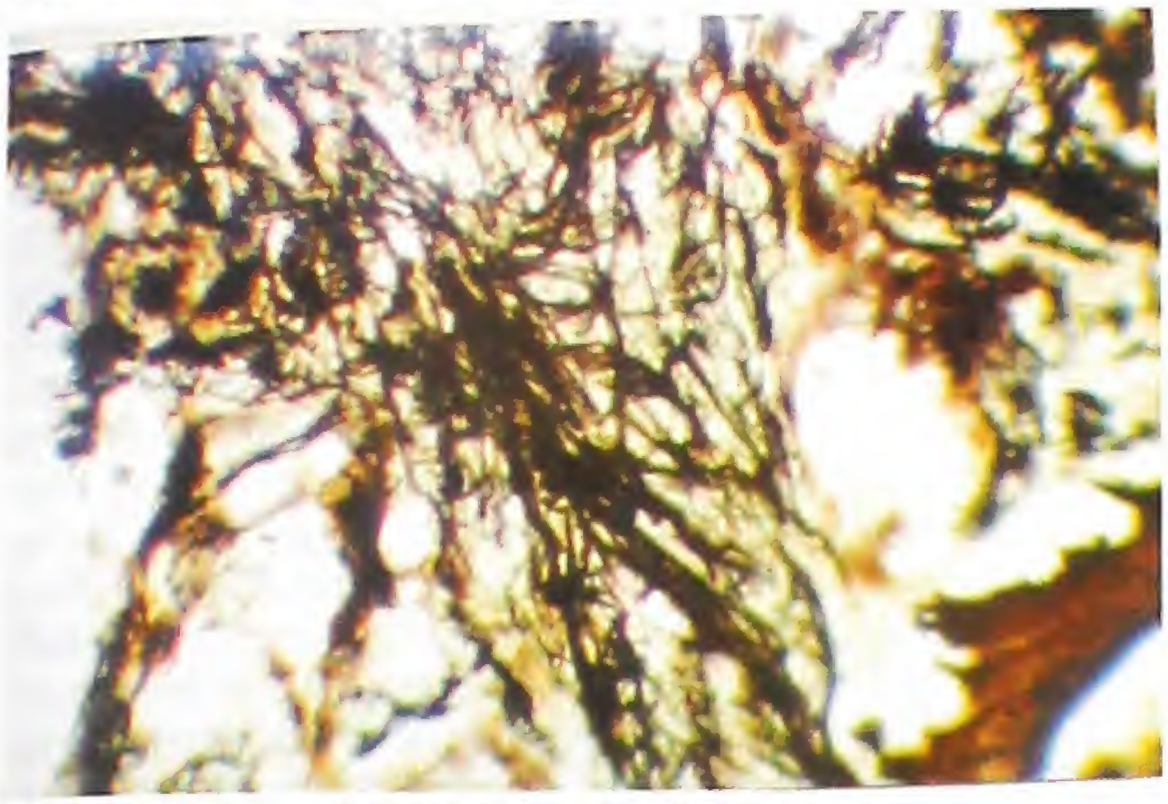

Figure 3. Silver impregtech. Section showing reticular fibrosis.

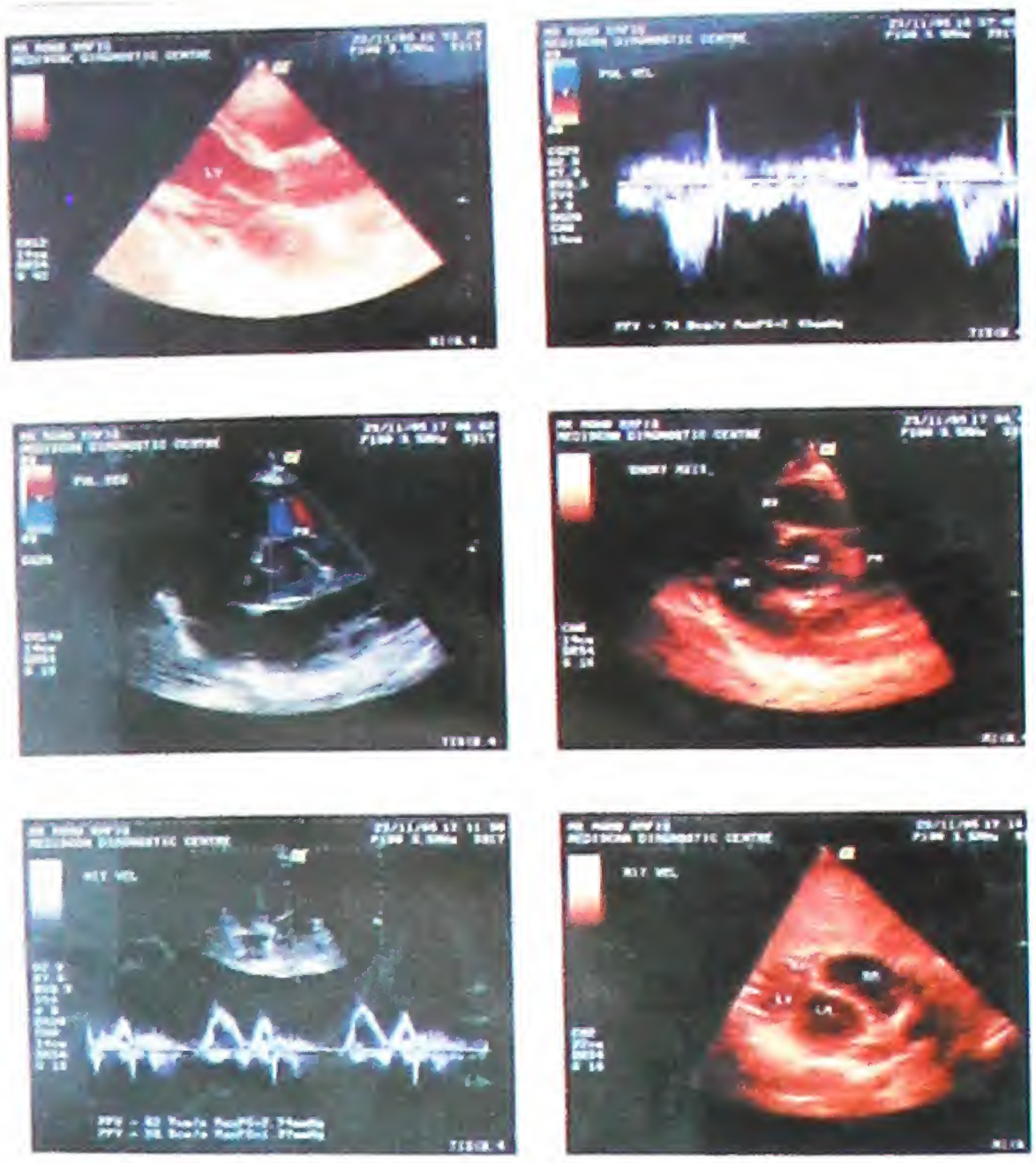

Figure 5. Ecocardiagraphy and Colour flow imaging.

Figure 4. MRI

hepatospleenomegly with no focal lesion. Spleen on RT and Liver on LT side (AP diameter 13 cm, cephalo caudal diameter 16.6cm. Stomach appears on midline.

2D Echocardiography & colour flow imaging showed

IVS-1.0cm	LVPwes 1.6 cm
LV ded-5.0 cm	Aorta :33 mm
LVPWed – 1.0cm	Laes : 41 mm
IV Ses 1.5 cm	FS : 39%
LVDes 3.1cm	EF :69%

EF= 72% (by Simpson's Method)
LVS-motion NR
Mitral value Morphology - NR
Aorta value - NR

MRI Revealed (Fig. 4):-

Situs Inversus

1) Liver lies on (Lt) side (enlarged)
   - Spleen on (Rt) side (grossly enlarged)
   - Gastric fundus (Rt) side

- pylorus on (Lt) side

2) Small leukemic deposits seen on a) dorsal spine (D3—D11)
b) S1 vertebra
c) (Rt) sacroiliac joint
d) (Lt) femoral neck

Treatment

Patient was shifted to Radiotherapy department GMC Jammu where he was given Cladribine (2- Chlorodeoxy adenosine) 0.9 mg /kg body wt daily for 7 days as I/v infusion. But patient developed lymphocytopenia & then a colony stimulating factor was added to the treatment. He received full cover of antibacterial antifungal & antiviral therapy during his follow up period & the result was a good clinical response.

Final diagnosis:-Hairy cell Leukemia in patient of situs inversus totalis.

DISCUSSION:-

Hairy cell leukaemia is an uncommon form of chronic B-cell leukaemia. In this there is clonal B cell Proliferation and it infiltrates into patient's reticuloendothelial system and interferes with bone marrow function resulting in pancytopenia. It also infiltrates in spleen and liver resulting in organomegaly.Hairy cell leukemia accounts for 1-2 % of all leukemic cases with male to female ratio of 5:1 and occurs primarily in male with median age of 52 years[1]. Although association of hairy cell with dual hematological malignancies like myeloma and T cell leukaemia is reported[2] but no association has been found with situs inversus.

Situs inversus occurs in 0.01% of population[3,4] with equal male to female ratio and in it situs describes the position of cardiac atria and visceras. Situs solitus is normal position and situs inverses is the mirror image of situs solitus. In situs inversus, the morphologic right atrium is on the left and morphologic left atrium is on the right. The normal pulmonary anatomy is reversed so that the left lung has 3 lobes and right lung has 2 lobes. In addition the liver and gall- bladder are located on left while spleen and stomach are located on right. The remaining internal structures also are a mirror image of normal. Situs inversus can be classified further into situs inversus with dextrocardia (situs inversus totalis) or situs inversus with levocardia. When situs cannot be determined, the patient has situs ambigous or heterotaxy. In theses patients liver may be midline, spleen absent or multiple, the atrial morphology unclear and the bowel malrotated. Situs inversus is associated with increased incidence of congenital heat diseases usually transposition of great vessels. Its association is also explained with kartagener syndrome in which there is bronchiectiasis, sinusitis. Also there may be nasal polyps, impaired sense of smell, recurrent otitis media and reduced fertility.[5]

Hairy cell leukaemia usually present with spleenomegaly (72-86%) left upper quadrant pain (5%), pancytopenia, leucocytosis (15-20%), neutropenia (32-39), heptomegaly (15-20%) Thrombocytopenia (53%) cutaneous vasculitis, lymphadenapathy (10%) & lytic bone lesion[6,7].

The typical Hairy cells are named because of their characteristic cytoplasmic projections which appear as fine (hair like) microvillae. When seen by light microscopy, phase contrast & electron microscopy. They are mononuclear cells with eccentric or centrally placed nucleus. Hairy cells have a mature B-cell phenotype and typically express single or multiple immunoglobulin light chains and pan-B-cell antigens as CD19, CD20, & CD22 but not CD21[8]. Cytochemical evaluation is important for diagnostic confirmation of morphological findings. HCL cells demonstrate strong positively for tartrate resistant acid phosphatase (TRAP) staining. Bone marrow aspirate usually is unsuccessful due to dry tap. Core biopsy of bone marrow shows a pattern of HCL infiltration with a single round or oval nucleus separated by abundant cytoplasm in a fine fibrillar network appearance which is diagnostic of hairy cell leukemia[9].

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Palatal myoclonus

Manjeet S. Bhatia, Ravi Gupta, Lakshmi Vaid

The reports of psychogenic movement disorders are few[1,2]

Psychogenic myoclonus represents the most common type of nonorganic movement disorder, accounting for over 8.5% of all patients with myoclonus and about 20% of all psychogenic movement disorders seen in a study[1].

Psychogenic origin is suspected when the distraction reduces movement, other psychopathology is present, or the symptoms respond to placebo or spontaneously, improvement occurs faster then expected by the therapy [1].

Palatal myoclonus has been reported after stroke[3], brainstem lesions[4], extirpation of cerebellar astrocytoma[5] or as epilepsy patialis continua[6].

Though psychogenic myoclonus has been described in different parts of body, palatal involvement has not been described in detail and there is scarcity of literature and only one case report of psychogenic palatal myoclonus could be traced[7].

A 30-year-old male presented in otorhinolaryngology department with the complaints of headache, difficulty in speaking due to abnormal palatal movement for six months. The severity of symptoms increased during the periods of stress and he did not provide any history that could suggest presence of neurological pathology. His otolaryngological and neurological examination, EEG, CT scan of head did not detect any abnormality. The patient was started on carbamazepine 400 mg per day and lobazam 5 mg per day but the episodes continued even after four weeks of therapy.

Psychiatrist's opinion regarding his symptoms was taken and a diagnosis of Adjustment disorder with anxiety was made. He was prescribed 1 mg Alprazolam per day with psychoeducation. Anticonvulsants were gradually tapered over 4 weeks. His family was also educated regarding the symptoms and stressors were taken care of by relaxation exercises and improvement of interpersonal communication in family. Patient started showing improvement after a week of initiation of psychiatric treatment. He was followed up upto 3 months but never developed same symptoms again.

To treat such problem, the patient should be educated about the illness, its causation and outcome. Supportive psychotherapy is usually used in the initial stages. Confrontation and psychotherapy has been found useful in over 75% patients as found in the present case. Behaviour therapy, hypnosis, family therapy and anxiolytic drugs are also used in selected cases.

Acute onset, short duration of symptoms, healthy premorbid functioning, and absence of coexisting organic psychopathology, presence of an identifiable and removable stressor and good family support and cooperation are related to better prognosis.[8,9]

Psychogenic movement disorders offer a clinical challenge to be correctly recognized and properly treated so that the patients are not exposed to unnecessary investigations and therapeutic dangers.

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Catastrophic Haemorrhage after the rupture of Rudimentary Horn Pregnancy

Indu Koul, Ajay Wakhloo,Shashi bala Gupta,Sapna,Rekha Jad.

There is risk of pregnancy developing in rudimentary horn from transperitional migration of sperm or ovum from opposite side. O'leary and O'leary[1] found corpus luteum to be on the side contralateral to rudimentary horn containing a pregnancy in 8% of cases. Signs and symptoms of an ectopic pregnancy will develop with eventual rupture of the horn if pregnancy is not detected early. Rupture through the wall of the vascular rudimentary horn is associated with severe intraperitorneal hemorrhage and shock . Therefore removal of the rudimentary horn is required as soon as a pregnancy is confirmed. Most pregnancies in a rudimentary horn rupture in the first or second trimester. Fedele and associates[2] have found ultrasonography useful in determining the presence of rudimentary horn.

We report a 26 year old , at 16 weeks of gestation presenting with an acute onset of pain abdomen , vomiting and giddiness on 2/7/2005 in SMGS hospital, Deptt of Obstetrics and Gynaecology under MRD No 841546 Her LMP and EDD was not known. She was G3 and P2. P1 – Full term normal delivery at home, baby died at the age of 3 months.P2-Full term normal delivery occured at home 1½ years back. Patient was afebrile, Pallor was +++ and pulse 100/min B.P 98/60 mm of Hg. Chest/CVS –NAD, Guarding was present. Cervix Soft , uterus size could not be made out. Bleeding per vaginum slight. Urine for pregnancy test was positive. Her blood group was A+ve and her haemoglobin was 6gm.Paracentesis was done which showed frank blood. Three blood pints were arranged and emergency laprotomy was performed Upon laprotomy, significant haemoperitoneum was encountered with the twelve weeks fetus floating in the abdominal cavity.Presence of ruptured left rudimentary horn with placenta in situ was encountered . The ruptured rudimentary horn was excised. In the postoperative period, the patient recovered uneventfully and was discharged on 8th post operative day.

Rudimentary uterine horn pregnancy is a very rare condition. Unicornuate uterus with rudimentary horn is a mullerian anomaly associated with endometriosis and pregnancy complications including miscarriage, eptopic pregnancy, uterine rupture, preterm labour and malpresentations. Therefore , the horn is removed if it is thought to contain functional endometrium .This is usually done by laprotomy in the non- pregnant state

According to Holden and Hart[3], some 350 cases of pregnancy in a rudimentary horn have been reported since the original case report by Maricean in 1669. Signs and symptoms of an ectopic pregnancy with eventual rupture of horn occur if the pregnancy is not detected early. Soundarajan and Rai[4] reported a case of rudimentary uterine horn pregnancy mimicking an ectopic pregnancy. In this case, horn was removed laproscopically .

In 1998, Dicker et al[5] reported the case of women who benefited from laproscopic surgery of a rudimentary horn. Laproscopy in this exceptional case was said to be most accurate diagnostic tool that gives significant advantages in efficient surgical management , there by avoiding laprotomy

Also in1998, Yahata et al[6] reported laproscopic management of uterine horn pregnancy mimicking an ectopic pregnancy but in this case, a rudimentary horn pregnancy was detected from transvaginal ultrasonography.

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Tumorigenic potential of STAT Proteins in Breast Cancer

Mohamad Ajaz Ul Haq Bulbul, Paul Laporte, Mohammad Muhsin Chisti

Introduction

STAT (Signal Transducer and activator of transcription) proteins are a family of 7 members of Cytoplasmic proteins that function as **secondary messengers** and transcription factors. The Stat proteins are unique among transcription factors in containing an SH2 (src-homology 2), phosphotyrosine binding domain. *The SH2 domain interacts with tyrosine phosphorylated site on receptor associated JAK to recruit the Stats that bind to them.* The potential of the SH2 domain to interact with a number of signaling proteins allows the Stats to interfere with multiple signaling pathways[1] They were originally discovered and characterized through the study of Interferon-induced responses[2]. They play a fundamental role in normal cell signalling in response to cytokines and growth factors. *In recent years, the constitutive or increased expression of JAK/STAT's has been found in cancer cells and oncogene transfected cells of cell lines, indicating their role in oncogenesis and its feasibility in therapeutic targeting in the future.* Their role in immune rejection of allografts and the inflammatory processes of autoimmune diseases is also being defined.

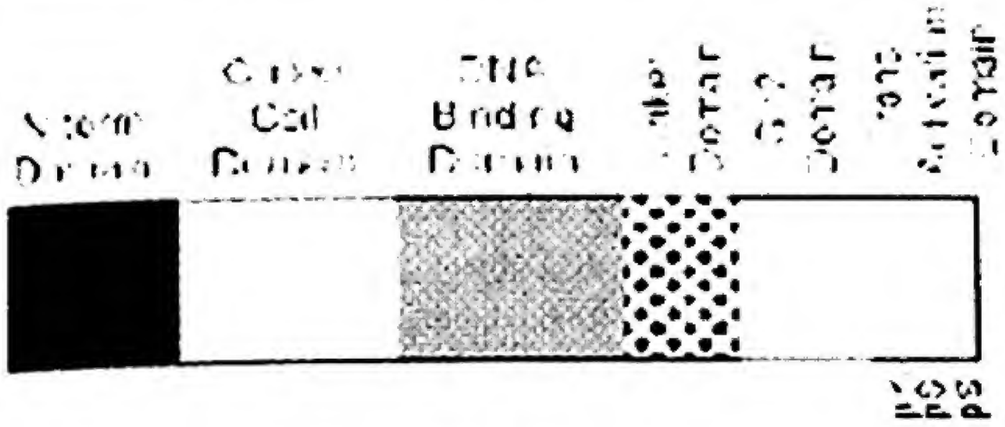

Fig 1: Structural map of STAT protein.
Py (Phosphorylated tyrosine residue), pS (Phosphorylated serine residue) at the non conserved carboxy terminal domain [3]

The JAK/STAT pathway includes seven functionally related, latent transcription factors (STAT) located on three different chromosomes and four non-receptor tyrosine kinases (JAK). Seven Stats (Stats 1–6, including two Stat5 genes) in mammals and range in size from 750 to 900 amino acids. Stats studied in model eukaryotes, like *Dictyostelium*, *Caenorhabditis elegans*, and *Drosophila*, are most closely related to mammalian Stat3 and Stat5 and appear to regulate developmental processes.[4].

In the typical JAK/STAT paradigm, a cytokine binding to its receptor results in activation of receptor-associated JAKs. After binding of a cytokine or growth factor to the receptor on cell surface, there's either activation of Cytoplasmic tyrosine kinases (particularly JAK or Src kinase families) or activation of receptor-intrinsic tyrosine kinase activity (such as those for EGF or PDGF). This phosphorylation event occurs adjacent to the transcriptional activation domain within Stats (at position 705 in Stat3 and Y694 and Y699 in Stat5a and Stat5b, respectively). Via whichever route, the dimers then translocate to the nucleus by poorly understood mechanisms, and bind to STAT-specific DNA consensus motifs called gamma-activated sites (GAS), of target genes to induce transcription JAK's then phosphorylate the Cytoplasmic receptor chains creating docking sites for recruited STAT's. Finally, STAT's are phosphorylated on tyrosine by JAK's, dimerize, and then translocate to the nucleus to activate specific target genes. Because the second messenger (STAT) is also the terminal transcription factor, in many ways the JAK/STAT pathway represents a streamlined apparatus for cellular signalling. Cytokines that activate STAT3 include growth hormone, IL-6 family cytokines, and G-CSF. **STAT3, as well as STAT5, induces progression through the cell cycle, prevents apoptosis and up regulates oncogene, such as c-myc and bcl-X and may play a role in oncogenesis**. STAT3 has been shown to play a critical role in haematopoiesis. The importance of STAT3 is underscored by the failure of mice lacking STAT3 to survive embryogenesis. Crosstalk from pathways other than JAK kinases also leads to phosphorylation and activation of STAT3 as indicated by a role of mTOR (mammalian target of rapamycin, or p70 S6 kinase) and MAP kinase pathways in STAT3 activation and signalling.[5].

It has been established that besides signaling functions in normal cells, STATs can also participate in oncogenesis[6]. Initially, the JAK family of tyrosine kinases was identified as the primary mechanism of STAT activation. More recently, a number of reports have correlated STAT activation with the activity of non-receptor protooncogenic tyrosine kinases (v-Src, v-Abl, Lyn, Lsk , Bcr/Abl, and Fes) by passing JAK kinases. STAT3 activation has

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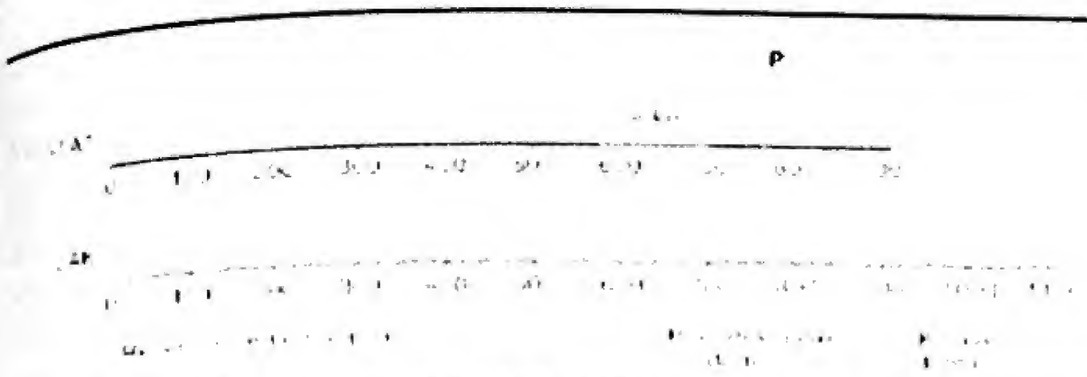


Fig 4: JAK/STAT structure: The STATs share several conserved domains, an amino-terminal domain (NH2), a coiled-coil domain, the DNAbinding domain, a linker domain, an SH2 domain, and a tyrosine activation domain (P). The carboxy-terminal transcriptional activation domain is said to be conserved in function, but not in sequence. Likewise, the JAKs share seven regions of high homology, JH1JH7. JH1 has been shown to encode the kinase. JH2 represents a pseudokinase domain, which appears to regulate JH1 catalytic activity. JH3JH7 have been implicated in receptor association.

Positive regulation of STAT'S

Tyrosine Phosphorylation: Activation of STAT requires the C-terminal tyrosine residue phosphorylation by receptor associated Janus Kinases[15,16] this in turn results in dimerization/multimerization and translocation into the nucleus for transcriptional activation.[17]. Tyrosine phosphorylation is necessary for Stat activity; replacement of this tyrosine residue results in an inactive Stat incapable of nuclear translocation or transactivation. However, other tyrosine kinase-signaling pathways may also impact Stat activation because both Stats 3 and 5 can be phosphorylated by Src family members[18].

Serine Phosphorylation: All Stat family members, with the exception of Stat2, undergo serine phosphorylation after receptor- mediated signaling. Serine phosphorylation at residue 727 of Stats 1 and 3 results in a significant up-regulation of the transcriptional activity of these Stats. This event appears to be mediated by several converging kinases including MAPK, p38, JNK, and protein kinase C. ***Serine phosphorylation of Stat3 appears essential in vivo for postnatal survival and growth.*** *Small GTP binding proteins* **Rac and Rho are capable of up-regulating Stat3 serine phosphorylation and transactivation**[1].

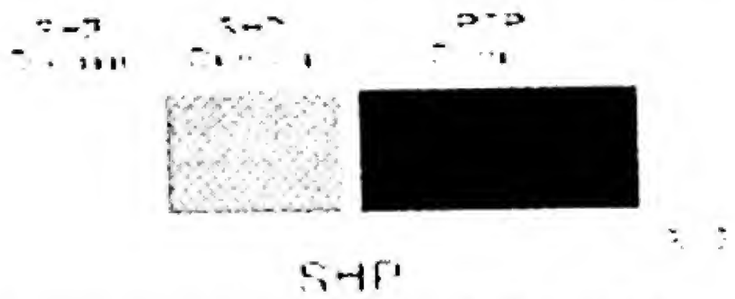
Serine phosphorylation appears to have a dual role in STAT regulation. Serine phosphorylation at positions 725 and 779 in Stat5a and position 730 in Stat5b down regulates the transcriptional activity of Stat5. Serine phosphorylation of both Stat5a and Stat5b appears to be increased during late pregnancy and lactation[19] The phosphorylation of serine 725 and 779 of Stat5a is mediated by both cross talking with MAPK and non-MAPK signaling pathways; On the other hand, the suppressive effects of this phosphorylation appears to be moderated in part by co-stimulation of glucocorticoid receptors in MCF7 breast cancer cells[19]. This issue remains contentious, in part because different serine kinases have been found to phosphorylate Stat1 and Stat3 depending on the nature of the incentive and co-stimulus[13]. Studies showed that serine phosphorylation enhances transcriptional activity of Stat1 and Stat3[13]. Some indicate that serine phosphorylation enhances Stat4 transcriptional activity[20]. Stat5, serine phosphorylation appears to enhance protein stability[21].

Negative regulation of JAK/STAT

Ubiquitin-proteosome dependent degradation may also play a role in the down regulation of cytokine signaling. Suppressor of cytokine signaling (**SOCS**) proteins are widely present in cytokine-stimulated cells. Cytokine regulation can occur in three ways, massive, transitive and coordinative. **SOCS-1** is a commonly detectable negative regulator of JAK. The second inhibitor of the JAK/STAT pathway is **Bcl-6**, which normally functions as a *transcriptional repressor* by binding to **STAT6**. Bcl-6 knockout mice develop an inflammatory disease characterized by increased levels of IgE, which is analogous to human atopic skin disease. The third negative regulation point is the **pseudo-kinase, JH2 domain, of the JAK protein**. JAK/STATs are also negatively regulated by protein tyrosine phosphatases (**PTPs**), nuclear protein inhibitor of activated STAT (**PIAS**).[8]

Dephosphorylation

Down reglation by dephosphorylation has been studied and researched to a limited extent but shows promise in future targeted approaches to STAT regulation in breast cancer. Dephosphorylation carried out by phosphatases, notably SHP1, SHP2, CD45, PTP1B, and TCPTP[22] seem to regulate Jak kinase activity, and some linked to the Stat's. Typically, receptor-associating phosphatases contain tyrosine- binding SH2 motifs, a phosphatase



SHP

Fig 4: A structural example of a SHP phosphatase [3]

domain, and regulatory tyrosine residues that undergo variable phosphorylation. SHP1 expression is largely restricted to haematopoietic tissues, while SHP2 is more widely expressed[23]. Some studies have suggested that SHP1 and SHP2 directly interact with and dephosphorylate JAKs and Stat5 respectively[24].

Additionally, recent studies have indicated that the membrane-spanning phosphatase, CD45, negatively regulates JAK-STAT signaling stimulated by IL-3, IL-4, EPO and IFN-g[25]. These observations indicate that phosphatases play an important role in negatively regulating STAT dependent signaling.

TCPTP has been found to associate with Stat5a and Stat5b within the nucleus and induce their dephosphorylation and inactivation; interestingly the phosphatase activity of TCPTP is not required for the inactivation of Stat5-mediated gene expression[26] the over expression of PTP1B also has similar effects on Stat5a and Stat5b phosphorylation and activity; however, this phosphatase is Cytoplasmic[27] SHP2 has been found in association with Stat5a and migrates with Stat5 as a complex into the

nucleus. Interestingly, the intact phosphatase activity of SHP2 is required for Stat5 phosphorylation, suggesting that this phosphatase is not directly involved in the dephosphorylation/ deactivation of Stat5, but instead indirectly with the activated.

Positive regulation besides tyrosine kinase by serine kinases and interacting proteins chromosome modifying proteins shown to interact with a STAT (i.e. Stat2) were CBP/p300[28] numerous studies have described a strong interaction between STAT's and other transcriptional regulators IRF-9, NF- kB, Sp1, USF-1, PU.1 and the glucocorticoid receptor among others[8]

While signalling through the JAK/STAT pathway has been well-characterized in response to interleukins and interferons, there is emerging evidence that STAT's also mediate cellular responses to various forms of cellular stress. For example, STAT3 was recently shown to be serine phosphorylated by JNK during UV stress which had a predominately inhibitory role on STAT3 transcriptional activity[29] Most notably *STAT 3 and 5 are found constitutively activated in breast cancer*, head & neck cancer, melanoma, multiple myeloma, CML, and AML among other malignancies[30]

HUMAN TISSUE DATA

Approaches: Different approaches have been used to assess STAT nuclear localization and its phosphorylation, and DNA binding ability of Stats 3 and 5 in breast tissues being the interest of experiments. Immunohistochemical approaches have successfully measured Stat 3 and 5 levels in breast tissues, and correlated this expression with intranuclear localization.

The advantage of an immunohistochemical approach is its ease in application to large numbers of patient specimens. The disadvantage to this approach is the presumption that phosphorylation and nuclear localization equate to transcriptionally active Stat; Alternatively, the level of Stat DNA binding can be measured by electrophoretic mobility shift analysis (EMSA); although this is perhaps a better measure of Stat activation, it is time consuming and not amenable to small tissue samples[3]

Nuclear Localization of Stat

Significant elevations in the DNA-binding activity of both Stat3 and Stat5[31] were noted in a small sample of Malignant breast tissues when compared to normal tissues.

At the immunohistochemical level, two studies have examined Stat3 localization and phosphorylation. The first study[32] examined 62 malignant breast cancers and found increased levels of nuclear localized i.e., phosphorylated Stat3 in comparison to normal surrounding tissues.

Tyrosine phosphorylation is essential for the dimerization of Stats and the associated nuclear translocation of the STAT dimer. The Stats contain no obvious nuclear translocation sequence, and the Stat domains involved in this critical event are largely unknown.[33]

In another study by Cotarla et al the pattern of Stat5a cellular localization was analyzed by immunohistochemistry in a series of 83 randomly selected primary human breast adenocarcinomas. Immunoprecipitation/Western blotting and immunohistochemistry assays employing different phospho-specific antibodies verified Stat5a tyrosine phosphorylation status. Stat5a was nuclear localized and tyrosine phosphorylated in 59 of 78 (76%) breast cancers examined; 38 of 78 (49%) demonstrated Stat5a nuclear localization in more than 25% of the breast cancer cells within the adenocarcinoma.[33]

The positive association with nuclear localized p27, a recently identified marker of differentiation for breast cancers[34], supported the positive association between nuclear localized and tyrosine phosphorylated Stat5a and increased levels of histologic differentiation. It is noteworthy that this is consistent with what is known about the role of Stat5a in normal mammary gland development. Activated Stat5a is required for the functional differentiation of mammary epithelial cells and lactogenesis during pregnancy and lactation[35]

Previously, it was presumed that whereas both signal transducers and activators of transcription (STAT) 5A and STAT5B can be activated only STAT5B was translocated to the nucleus, where it presumably activates distinctive transcriptional responses.[6]

Another study[36] evaluating a microarray containing tissues from 346 node-negative breast cancer patients with both anti-Stat3 and anti-phospho-Stat3 immunohistochemistry and correlated these results with clinicopathological and survival data. This study revealed that nuclear Stat3 and phospho-Stat3 was noted in 23% and 44% of patients, respectively; the incongruity of the study wasn't remarked on. **Multivariate analysis** of these data revealed that this parameter was statistically a better predictor of tumor outcome than tumor size, nuclear grade, age, estrogen/progesterone receptors and Her2 Status, and Ki-67 positivity.

There is a significant intranuclear Stat5 presence in both normal and lactating human breast tissues; parallel studies in mice confirmed this theory that a basal level of Stat5 phosphorylation can be noted in normal virgin, pregnant, and lactating mammary glands[37]. Whether the phosphorylated Stat5 in the nonpregnant, normal breast is actually bound to DNA and transcriptionally active (or bound to a repressors) hasn't been determined. A more recent study examining more than 1300 breast cancers has found a strong association between Stat5 nuclear localization/phosphorylation and improved overall and disease-free survival[38]

An *in vivo* study on relationship between Stat phosphorylation and DNA binding[39]. evaluate Stats 1, 3, and 5, found a strong correlation between Stat 1 and 3 phosphorylation (measured by Immunoblot analysis) and DNA binding (as measured by EMSA) in human tissues, but could not detect Stat5 phosphorylation, possibly secondary to technical difficulties with antibody difficulties. Although the study found a correlation between Stat1 activation/phosphorylation and survival

(but not Stats 3 or 5), the numbers of this study were small (68 samples including both node-negative and node-positive), the data were not **Normalized** to total Stat content, and Stat phosphorylation was not assessed by immunohistochemistry (i.e., the contribution of inactive Stat could have been telling). To date possibly no study has reported on Stat localization/ phosphorylation in the nonepithelial connective tissue compartment of normal or malignant breast tissues, or in various histopathological subtypes of carcinoma breast.

Mammalian studies on mouse

Gene targeting studies have suggested that Stat5 plays a critical role in lobuloalveolar proliferation, differentiation, and expansion, whereas Stat3 regulates lobuloalveolar apoptosis during pregnancy, lactation, and involution.[40]. *In vivo*, the effect of hemizygous loss of Stat5a in a SV40-T antigen transgenic mouse model of mammary cancer has been tested after cross-breeding. The resultant progeny (Stat5a_/__ Tag) demonstrated a significant reduction in mice tumors, as well as decreased tumor size, delayed first tumor appearance, and increased apoptotic indices[41] The role of Stat3 in murine mammary cancer models isn't obvious and awaits further cross-breeding experiments[40]

Cell line experiments

As seen with in-vivo studies. Stat3 tyrosine phosphorylation and DNA-binding activity of several breast cancer lines has been found to be elevated; & conversely, pharmacological or dominant-negative inhibition of Stat3 activity has been found to block the proliferation and survival of breast cancer cells *in vitro*[42] [43] Stat5 has been demonstrated to stimulate the transcriptional activity of the cyclin D locus[45]. Transfection of a constitutively activated Stat5 resulted in growth factor-independent growth of the murine Ba/F3 pro-B cell line[46] and over expression of Stat5b has been found to potentiate v-src-mediated transformation of NIH-3T3 cells[47] Repression of Stat5 DNA-binding activity by PIAS3 inhibits breast cancer cell growth[47] . STAT5B in cell lines accelerated v-Src-inducible transformation. When NIH-3T3 (Embryonic fibroblast; Mouse Cell line) cell lines were stably cotransfected with various combinations of different forms of STAT5 and oncogenic v-Src kinase[47]

A number of different studies have also demonstrated the direct participation of STAT3 in transformation in response to Src kinase activation in NIH-3T3 cells. Therefore, there is a possibility that STAT5B and STAT3 may cooperate in the process of transformation. Further studies may be required.

Collectively, many studies have argued for a significant role for Stats in breast cancer proliferation, survival, and differentiation. The mechanisms through which the Stats promote these pro tumorigenic events has been an active area of investigation; Varied evidence indicates that Stats 3 and 5 can activate the transcription of genes associated with cell-cycle progression, cell survival, transformation, and angiogenesis required for its incessant growth and spread as elaborated in recent reviews[48] [49] Research shows Stat3 and Stat5 activity in the up-regulation of expression of the cell cyclin D1 and D2 in several non mammary cell lines. However, only a single research to date has suggested that Stats may have similar effects in breast epithelial cells[45]. Regulation of anti-apoptotic members of the Bcl-2 family, specifically Bcl-XL, has also been associated with Stat3 and Stat5 activity[48] [7]

Conclusion

The JAK/STAT pathway plays a central role as messengers and integrators of cytokine signaling from multiple pathways. Research indicates the association of Breast Cancer with that of nuclear localization of phosphorylated STAT and its relation to histological differentiation. There is a vast array of interactions between JAK/STAT and modifier proteins. tumorigenic potential of Stat's in breast cancer makes them a target for future use as prognostic and therapeutic agents in Breast Cancer. It is conceivable that specific inhibitors of Stat phosphorylation/activation and/or dephosphorylators of Stat's could lay the ground work for regulation of Stat activity in Human Breast Cancer.

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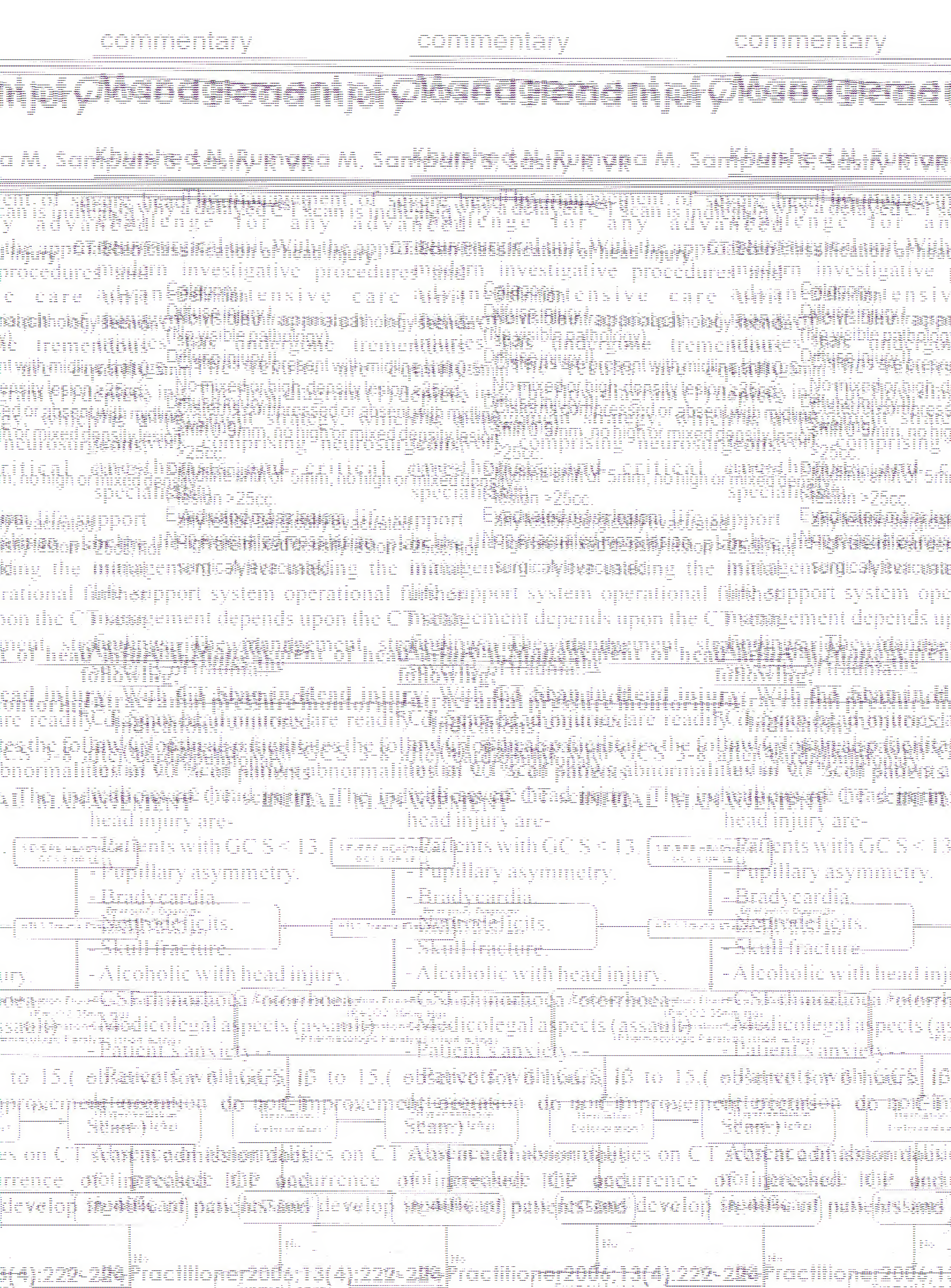
ABBREVIATIONS

MAP Kinase - Mitogen Activated Protein Kinase, SHP - Sre Homology Phosphatase, PTP - Protein phosphotyrosine phosphatase TCPTP - T-cell protein tyrosine phosphatase, V-SRC - The Rous Sarcoma Virus (RSV), CD-45 - Cluster differentiation Bcl-B Cell lymphoma, STAT - Signal Transducer and activator of transcription



(2) Unilateral or bilateral motor posturing.
(3) Systolic B.P < 90mm Hg.

Less than 3% of patients with GCS 13 – 15 and 10 % with GCS 9-12 will deteriorate and need ICP monitoring.

Control of raised intracranial pressure.

(a) **Pharmacotherapy :-** Mannitol is still the drug of choice for raised intracranial pressure . The recommended dose is 0.25g / kg - 1g / kg. It has both immediate and delayed effects. It has a plasma expanding effect and it reduces blood viscosity hence increases cerebral blood flow and cerebral oxygen delivery. It improves the plasticity of RBC'S which again helps in oxygen delivery. Delayed effects start after 15 –30 minutes. Mannitol increases the osmolarity of serum and hence by way of osmosis draws out water from brain. The delayed effects last up to 6 hrs. The side effects of mannitol are acute tubular necrosis, hyperkalemia and acidosis.Frusemide, a loop diuretic causes super additive lowering effect if given with mannitol. It may be useful when the response to mannitol is unsatisfactory. The recommended dose is 1mg/kg/dose. If pharmacotherapy fails further methods to reduces the ICP include, the below mentioned methods.

(b) **Hyperventilation:-** once considered among first line defense measures against raised ICP, is now regarded as a method to be used in moderation only and in specific situations. Prophylactic hyperventilation is actually associated with a poor outcome. When indicated hyperventilation should only be used to keep pco = 30-35mmHg. Hyperventilation to p.co < 30mmHg further reduces CBF but does not consistently reduce ICP and may cause loss of autoregulation.

(c) **Hypothermia:-** temperature of 32-34°c is maintained for at least 48 hours and is to be started within 8 hours of traumatic brain injury (TBI). Potassium supplements need to be given during hypothermia induction as it induces hypokalemia.

(d) **Barbiturate coma:-** is induced for depression of metabolic activity which indirectly reduces cerebral blood flow coupling. A loading dose of 10mg/kg of pentobarbital over 30min then infusion of 5mg/kg/hour for next 3 hour then 1mg/kg/hour. The dose can be increased to 2 –3mg/kg (Eisenbergs protocol). The goal of the therapy is to achieve burst suppression of EEG and ICP control and if burst suppression has been achieved but ICP is still high, high dose barbiturates are given to cause electrocerebral silence. Serum levels of 3-4mg% correlate well with adequate physiologic response. When adequate ICP control has been obtained for 24-48hours, the therapy is tapered under cover of analgesia and sedation.

(e)Decompressive craniectomy: - The last a lost resort after failed conservative management either unilateral or bilateral craniectomy can be done.

Though there is institutional variation to control the ICP the protocols for ICP management described by Rosen and Lundh are hereby enumerated.

Rosners protocol: - According to him ICP does not need treatment as long as cerebral perfusion pressure (CPP) is maintained at 70mm Hg or higher. Hypervolemia has to be maintained and pressors be liberally used to maintain the CPP. However there is no randomized controlled trial to support it and critics says that effect of elevating CPP may simply be the avoidance of hypotensive episodes and not related to increased cerebral blood flow (CBF).

Lundh protocol :- it is based on Starling model for vasogenic edema. The aim is to increase hydrostatic and osmotic forces favouring maintenance of fluid within the vascular compartment. α blockers and centrally acting ά-agonists are used to maintain cerebral perfusion pressure. A negative fluid balance is aimed at, to increase serum osmolality. Albumin and plasma are used liberally for fluid resuscitation. This protocol also lacks support of a randomized controlled trial.

(B) Further management of head injury patient: -

After initial management further management includes;

(a) Anti-seizure prophylaxis: - Risk factors for seizures are-

- GCS <10.
- Contusion /intracerebral hematomas .
- Subdural hematoma.
- Depressed fracture.
- Seizure within 24 hours of injury.

Children are at greater risk during first 24 hours and anti seizure prophylaxis is recommended for early seizures i.e. occurring within one week of head injury. No drug is effective for late seizure, if late seizure occurs patients should be maintained in accordance with standard approaches to patients with new onset seizures.

(b) Nutrition: in a head injury patient the metabolism increases by 40% metabolic derangements include increased levels of catecholamines, insulin, glucagons, cortisol, IL –1, IL-6, hyperglycemia. Hyperglycemia cause secondary neuronal damage by aggravating cerebral acidosis. There is increased urinary nitrogen loss suggesting catabolic state. It has been reported in one series that 75% of patients with admission serum albumin ≤ 2.5g% had unfavorable out come while only 38% with >2.5g% had unfavourable outcome (McClain). Patients who are started on nutrition earlier have better out come than when it is started later.

The energy expenditure required is as: -

Males - $66.47 + 13.75 \times W + 5.0 \times H - 6.76 \times A$.
Female - $65.75 + 9.56 \times W + 1.85 \times H - 4.68 \times A$.
Infrants - $22.1 + 31.50 \times W + 1.16 \times H$.

W = Weight in Kg's.
H = Height in Cm
A = Age in years.

Prognosis in severe head injury :- there are several factors determining the outcome in head injury patients . In elderly >65 years of age mortality is twice than in younger patients. Children <5 years have better outcome than older children. A positive alcohol screen has bad outcome. One episode of hypotension doubles the mortality rate. 82% of patients with GCS >11 have good outcome and 87% of patients with GCS of 3 will die.

One of the severe types of head injuries is **Diffuse Axonal Injury** which is defined by the following criteria;

- Lesion in corpus callosum
- Axonal rolling of white matter.
- Contusion in dorsolateral

quadrant of brain stem.

This injury occurs in 50% of severely head injured patients and accounts for 35% of all death from head injury. Besides the usual management of head injury patients' further therapies for DAI includes anti-cholinergic and anti-inflammatory agent, calcium channel blockers, free radical scavengers and lipid peroxidation inhibitors including cyclo- oxygenase inhibitors like ibuprofen or indomethacin and 12-aminosteroids such as .trilizide. Durgs, which cause presynaptic inhibiton of glutamate release such as lamotrigine and riluzole have also been tried under experimental circumstances. Other drugs include neurotrophic and polypeptide growth factors such as nerve growth factor and fibroblast growth factor

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Polyglandular Disorders

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Introduction:

Although endocrine glands are widely dispersed in the human body but it has been found that in certain conditions, they may get involved in the disease processes simultaneously

Endocrinology is fast emerging as one of the most developing branches of medical sciences and with simultaneous development of advanced radiological techniques, we can better go into the details of endocrine glands. Doctors need to recognize diseases that involve independent abnormalities of more than one endocrine gland for a number of reasons:

1. *First, the known patterns of multiglandular disease can alert the clinician to look for a second disorder when one is diagnosed.*
2. *Second, the treatment of many of the individual diseases in polyglandular disorders may differ from the treatment appropriate for the same diseases when they present in isolation.*
3. *Third, because many of these diseases appear in characteristic familial patterns, the recognition of the syndromes can lead to useful family screening.*
4. *Fourth, an understanding of the pathogenesis of these unusual disorders is likely to clarify the pathogenesis of more common single-gland disorders as well.*

Poly glandular Neoplasia

Three mechanistically distinct neoplastic syndromes involve more than one endocrine gland. Although given a variety of different names in the past, they are now most frequently called

- ***Multiple endocrine neoplasia type 1***
- ***Multiple endocrine neoplasia type 2a***
- ***Multiple endocrine neoplasia type 2b***

Auto immune Poly glandular Syndromes

- ***Auto immune Polyglandular Syndrome1***
- ***Auto immune Polyglandular Syndrome2***

Simple: Mc Cune Albright Syndrome

MULTIPLE ENDOCRINE NEOPLASIA MEN Type I (Wermers Syndrome) is an autosomal dominant disorder characterized by hyperplasia or neoplasia of the **pancreatic** islets, the anterior **pituitary**, and the **parathyroids**. In most kindreds, hyperparathyroidism is usually the presenting manifestation, with a prevalence approaching 100% by 50 yr of age but occurring only rarely in children younger than 18 yr of age. **Less commonly, adrenal gland neoplasia, foregut carcinoids (primarily of thymus and lung), and lipomas occur**. Because thyroid neoplasms are so common in the general population, their true association with MEN 1 is debated.

Parathyroid Disease. **Hyperparathyroidism** is the most common abnormality in MEN I, found in more than 90% of patients. Elevation of blood calcium generally first appears between the ages of 20 and 40, considerably earlier than in sporadic primary hyperparathyroidism; this is not a disease of children, however. At first, the disease is asymptomatic but then can lead to all the expected consequences of primary hyperparathyroidism. Unlike sporadic hyperparathyroidism, the disease is relentlessly progressive and, with prolonged follow-up, always involves all four parathyroid glands.. If fewer than three parathyroid glands are removed, hypercalcemia always recurs, although not necessarily immediately. Surgical results in MEN I are generally less satisfactory than in sporadic four-gland parathyroid disease. At some centers all four glands are removed, and a portion of one gland is reimplanted in the easily accessible forearm in an attempt to avoid the hazards of too much or too little surgery..

Pancreatic Islet Disease. As many as 80% of patients have pancreatic abnormalities at autopsy; a large number correspondingly have **increased blood levels of gastrin, insulin, pancreatic polypeptide, somatostatin, vasoactive intestinal polypeptide, or glucagon during stimulation or suppression tests.** The pancreas is often diffusely involved **with microadenomas and macroadenomas** and **hyperplastic lesions**. Characteristically, more than one islet hormone is secreted from these multiple tumors. Despite this underlying pattern of multiple cellular involvement, patients characteristically present with symptoms of only one hormonal disorder. The most common disease is **Zollinger-Ellison syndrome, peptic ulcer disease** associated with gastrin-producing tumors. The gastrinomas in MEN I are often multiple, very small, and found in the duodenal wall. Macroadenomas observed in the pancreas by computed tomography (CT) or intraoperative ultrasonography may well synthesize hormones other than gastrin.

Although some centers continue to experiment

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with aggressive attempts at surgical cure, the high recurrence rate after surgery has limited the role for surgery in this disease. Medical therapy with H2 receptor antagonists and H+,K+-ATPase eg **Roxatidine, Nizatidine, Rabeproazole, Pantaparezole,Lansaperazole,** etc are routinely used The tumors are slow-growing but frequently metastasize locally and to the liver. Chemotherapy is only partially effective and never cures the disease.

Insulinomas are the second most common clinically important islet tumor in MEN 1. These tumors are often small and multiple and are much less frequently malignant than the gastrinomas. Despite the frequently diffuse nature of the disease, dominant insulin-producing tumors can often be identified by **selective portal venous sampling**. Removal of the dominant tissue, or, if necessary, subtotal (80%) pancreatectomy is the primary therapeutic strategy.

Pituitary Disease. As in sporadic disease, pituitary disease can present with a **hypersecretion syndrome** or with symptoms due to a **sellar mass or hypopituitarism**. Pituitary tumors occur in more than half of MEN 1 patients. **Prolactinomas** are the most common tumors. **Adrenocortical hyperfunction** can result from a pituitary adenoma or from production of ACTH or corticotropin-releasing hormone by a foregut carcinoid. Although nonfunctioning adrenal neoplasms are common in MEN 1, **primary adrenal neoplasms** causing glucocorticoid excess are rare. **Acromegaly** can result from a pituitary neoplasm or as a consequence of production of growth hormone-releasing hormone by pancreatic islet tumors. After consideration of ectopic hormone and releasing hormone production by nonpituitary tumors, the course and treatment of pituitary disease in MEN 1 resemble those of sporadic pituitary disease.

Pathogenesis: Family studies have mapped the gene responsible for MEN 1 to the long arm of chromosome 11, band 11q13. Additional genetic abnormalities consist loss or mutation of DNA at loci that include 11q13.. The tumors are clonal expansions that may result from loss of function of a so-called tumor suppressor gene. Without identification of the gene, the identification of affected family members relies primarily on clinical screening. The most useful single test to complement a **thorough history and physical examination** is measurement of blood calcium, particularly ionized calcium, at intervals after age 15. **Prolactin, gastrin, and fasting blood sugar measurements** can also be useful.

MULTIPLE ENDOCRINE NEOPLASIA MEN TYPE IIA (Sipples Syndrome). When hyperplasia or carcinoma of C cells is associated with adrenal medullary hyperplasia or pheochromocytoma and parathyroid hyperplasia, it is known as MEN IIA. The inheritance pattern for MEN IIA is autosomal dominant, with a high degree of penetrance and variable expressivity; the gene (RET proto-oncogene) was assigned by linkage studies to chromosome 10q11.2, Multiple endocrine neoplasia type 2a is an autosomal dominant disease that presents with **medullary carcinoma of the thyroid (MCT), pheochromocytoma, and, less commonly, hyperparathyroidism**. Multiple endocrine neoplasia type 2b is closely related to MEN 2a because it also presents with medullary carcinoma of the thyroid and pheochromocytoma and because both diseases map to the same genetic region—the pericentromeric region of chromosome 10.

MULTIPLE ENDOCRINE NEOPLASIA (MEN), TYPE IIB. (Mucosal Neuroma Syndrome) The distinguishing feature of MEN IIB, also called the mucosal neuroma syndrome, is the occurrence of **multiple neuromas and a characteristic phenotype associated with medullary carcinoma and pheochromocytoma**. This condition is also autosomal dominant, and 93% of families have a missense mutation of the RET proto-oncogene. However, the mutation is in exon 16, the tyrosine catalytic domain of RET; all patients have had the same point mutation

MEN 2b presents with a number of abnormalities not found in MEN 2a, however. **These include mucosal neuromas of the tongue, lips, eyelids, and gastrointestinal tract and a marfanoid habitus.** Hyperparathyroidism rarely occurs in MEN 2b. MEN 2b is less common than MEN 2a; both diseases are rarer than MEN 1.

In MEN 2a and 2b, the medullary cancers and the pheochromocytomas often present bilaterally. Careful prospective analysis of MEN 2a families has demonstrated that diffuse C cell hyperplasia precedes clinically obvious appearance of medullary cancer by decades. C cell hyperplasia can be detected by measurement of calcitonin after administration of gastrin. With current sensitive assays, the median age of presentation with C cell hyperplasia is 8 or 9. Virtually all MEN 2a patients eventually develop C cell disease. Complete thyroidectomy of patients with C cell hyperplasia has dramatically decreased the incidence of medullary cancer, which has been the major cause of death in MEN 2a.

Half the patients with MEN 2a develop pheochromocytomas. Family screening allows the detection of pheochromocytoma before the development of hypertension. The first laboratory abnormalities noted include **an increase in urinary epinephrine and in the ratio of epinephrine to norepinephrine in the urine**. Increases in urinary metanephrine and norepinephrine come later. The tumors are usually found in the adrenal glands and can be **documented preoperatively by CT, magnetic resonance imaging, and [1311]-metaiodobenzylguanidine scanning.**

Most patients with MEN 2a have been found to harbor point mutations in the RET proto-oncogene.. In contrast to the pattern in MEN 1, no evidence for somatic mutations in the RET region of chromosome 10 have been found in MEN 2a tumors.. The mutant RET genes are, therefore, likely to be inherited oncogenes.

The transition from diffuse hyperplasia of C cells or adrenal medullary cells to clonal neoplasms of the thyroid or adrenal probably requires subsequent somatic mutations. Such mutations include the loss of genetic markers on chromosomes 1p, 3p, 3q, and 22q that frequently occur in these tumors.

Patients with MEN 2b harbor a point mutation

that changes methionine-918 to a threonine within the ret protein's intracellular kinase domain.

Carriers of the MEN 2 genes can best be identified by serial measurement of stimulated blood calcitonin levels, starting at an early age. Rapid progress in defining the RET lesions in MEN 2a now allows **direct genetic testing**, replacing calcitonin testing as a screening tool.

McCUNE-ALBRIGHT SYNDROME. McCune-Albright syndrome is the most dramatic example of a spectrum of disorders that vary in severity and presentation depending on the stage of development of the original mutant cell.

The McCune-Albright syndrome is a noninherited disorder consisting of the **triad of polyostotic fibrous dysplasia, light brown pigmented skin lesions (café-au-lait spots), and endocrinopathy, usually precocious puberty.** Multiple endocrine abnormalities can occur.

- The precocious puberty, more often seen in girls than boys, is gonadotropin-independent. Hyperthyroidism is caused by autonomous thyroid nodules.
- Acromegaly is caused by pituitary adenomas that produce growth hormone and, usually, prolactin.
- Adrenocortical hyperfunction is caused by ACTH-independent adrenal adenomas.
- Hypophosphatemic rickets, with normal blood calcium, phosphate wasting, and low or inappropriately normal levels of 1,25(OH)2D3, may result from release of a humoral factor from the dysplastic fibrous tissue.

The mutations in McCune-Albright syndrome are point mutations at arginine-201 in the GS a subunit; these mutations lead to prolonged activity of GS and inappropriate activation of adenylate cyclase. Increased levels of cyclic AMP lead to cellular proliferation and hormone secretion. McCune-Albright patients are genetic mosaics. Presumably, at an early stage in embryonic development, a point mutation occurs in the GS a gene of a cell that then proliferates, differentiates, and variably populates normal bone, skin, and endocrine tissues. In cell types in which elevations in cyclic AMP lead to proliferation, abnormal cells become predominant and lead to disease. Because the disease is never inherited, the mutation is presumably lethal when present in all cells of the embryo.

AUTOIMMUNE POLYGLANDULAR DYSFUNCTION

Organ-specific autoimmune disease, characterized by lymphocytic infiltration and organ-specific autoantibodies, commonly results in endocrine hypofunction or hyperfunction. Clinical manifestations of disease are usually limited to one gland. Not uncommonly, however, disorders of more than one endocrine gland appear in families or in individual patients. Characteristic patterns of disease presentation and genetic inheritance allow the definition of two syndromes with overlapping manifestations

AUTOIMMUNE POLYGLANDULAR SYNDROME TYPE 1.

This rare disease presents typically in early childhood. Autoimmune polyglandular syndrome type I is an autosomal recessive disorder. The appearance of organ-specific autoantibodies precedes disease presentation and predicts the development of specific end-organ damage.

Mucocutaneous candidiasis occurs in virtually all patients and is usually the first manifestation of disease. **Hypoparathyroidism** and **Addison's disease** are the most common endocrine manifestations; each of these diseases occurs in 70 to 80% of patients. Hypoparathyroidism usually precedes Addison's disease; both diseases typically present before age 15. **Premature ovarian failure (in 60% of affected women) usually presents as secondary amenorrhea; testicular failure occurs less frequently. Insulin-dependent diabetes mellitus occurs in 12% of patients, usually in adulthood; hypothyroidism is un-common.**

Nonendocrine components of this syndrome, in addition to the **mucocutaneous candidiasis, include alopecia, vitiligo, corneal opacities, autoimmune hepatitis, enamel hypoplasia of teeth, tympanic membrane calcification, nail dystrophy that correlates only loosely with obvious candidiasis, parietal cell atrophy and vitamin B12 malabsorption, and more general intestinal malabsorption with steatorrhea.** Asplenism, with Howell-Jolly bodies on peripheral blood smears, has been noted in several patients.

Each of the disease components should be sought when any patient presents with hypoparathyroidism, primary adrenal insufficiency, or mucocutaneous candidiasis. The hypoparathyroidism is treated like the sporadic disease with oral calcium and 1,25-dihydroxyvitamin D, although variable intestinal malabsorption can present a particular therapeutic challenge. The candidiasis can be satisfactorily controlled with **ketoconazole**.

AUTOIMMUNE POLYGLANDULAR SYNDROME TYPE 2. This syndrome is considerably **more common than the type 1** syndrome and typically presents in adulthood. **Insulin-dependent diabetes mellitus and thyroid dysfunction**—either autoimmune hypothyroidism or grave's disease—are the most frequent manifestations. **Addison's disease is the third major endocrine component of this disorder**. Although most patients who present with autoimmune diabetes or thyroid disease have clinical involvement of only one gland, a large fraction of patients with autoimmune addison's disease develop clinically evident disease in other endocrine glands. Less common components of the type 2 polyglandular syndrome include **primary hypogonadism and hypophysitis. Pernicious anemia, vitiligo, celiac disease, alopecia, and myasthenia gravis are also associated with this syndrome.**

The treatment of each component of this syndrome is identical to the treatment of each disorder in isolation, although possible clustering of diseases must be kept in mind during the evaluation and follow-up of all patients with each individual component disorder.

Autoimmune polyglandular syndrome type 2 is usually inherited in families with **characteristic HLA**

associations. Typically, several different autoimmune diseases occur in each family. Autoimmune vulnerability rather than specific organ disease is inherited

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Anaemia In Children - A Challenge

Aijaz Ahmad Lone, Shakir Ahmad Wani, Zubair Ashai, Fazal Q. Parray

Anaemia in children – A challenge

Anemia is the principal nutritional dearth in the world, and it especially affects children and pregnant women in developing countries. Nutritional Anemia according to the WHO, is a state in which the hemoglobin concentration in the blood is lower than levels considered normal for the age, gender, physiological state and altitude, as a consequence of shortage of essential nutrients, independent of the cause of this deficiency[1,2]. Nutritional anemia includes lack of nutrients such as iron, folic acid, vitamin B_{12} and copper, vitamin C and E and vitamin A[3].

The occurrence of anemia due to iron deficiency is labeled as iron deficiency anemia[4]. This deficiency is the most common nutritional disorder in infancy, and it affects communities not only in developing nations but also in highly industrialized countries[5,6]. Iron deficiency anemia also affects women of child bearing age[7,8].

Etiology

The main factors involved in the etiology of anemia in children are the iron reserved at birth, growth rate, diet and iron loss[9]. Organic physiological loss of iron occurs in bile, urine and cellular desquamation of the skin and intestinal lining. In children, loss also occurs due to blood in the feces and by the use of whole milk in liquid form during the first year of life[10,11]. Another possible cause of iron loss is the presence of intestinal parasites, although several studies have shown that the majority of parasitic diseases have secondary importance in the etiology of iron deficiency anemia in under 5-year olds[12-16].

The most significant weight gain and storage of iron by the fetus occurs during the last trimester of pregnancy. Premature births, intrauterine growth restriction and multiple pregnancies are factors that lead to iron deficiency anemia within the first six months of life, caused by low stocks of iron at birth[6,10]. The average iron concentration per kilogram of body weight at birth is 70mg/Kg for full-term infants[6,10]. The average daily iron needs are from 0.72mg to 0.46mg for children from five months to one year old and from one to three years old, respectively[17].

In the diet, the quantity of bioavailable iron is important, and this is determined by stimulation and inhibitory factors that exist within a meal[18]. Among the iron absorption stimulation fctors in the diet are organis acids, in particular ascorbic acid, which is found in citric fruits[18]. Among the iron absorption inhibitory factors are phytic acids, which is found in fibres, whole grains and beans[19], oxalic acid, which is found in spinach and beetroot[20], and tannin, which is found in tea, coffee and chocolate[21]. Calcium, which is present in milk and dairy products[22], and other minerals that are close to iron in the periodic table, which compete with the same intestinal absorption[23], also inhibits the absorption of iron.

For full-term newborn babies, the iron deposits at birth provide the needs for this mineral until four to six months of age. Breastfeeding alone acts as a protective factor during the first months of life and, in spite of the low iron content of human milk (0.26 to 0.73mg/L), the mineral in mother's milk has high biolavailability and absorption (around 50%)[24]. Because of the greater physiological requirements within the first two years of life, and specifically from 6 to 12 months because of the accelerated growth during this period, it is rare that the child will manage to ingest the recommended daily amount of iron. This is true even when good sources of bioavailable iron are introduced into the diet. Thus, preventive iron supplements are usually necessary for this age group[17].

Prevalence

According to the United Nations Childrens' Fund (UNICEF), 90% of all types of anemia in the world are due to iron deficiency[4]. In South and Central America, iron deficiency anemia has been a severe public health problem, affecting as many as 50% of pregnant women and children[7].

Consequences of iron deficiency in children

Studies show that children with iron deficiency present worse performance in psychomotor tests than do non-anemic children. The greatest prevalence of iron deficiency among breastfed infants coincides with the final period of rapid brain development (six to 24 months), when the motor and cognitive skills take shape. Long-term prospective studies have also identified persistent cognitive deficiencies in 10-year-old children who had suffered from anemia during the first month of infancy.

In South Africa, six to eight-year-olds who were observed to have low iron reserves, presented with

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retarded growth in comparison with those who had normal reserves. A boost in the growth of iron-defient preschool children was seen after supplementation of this mineral. Also, 12 to 18-month-old children with iron deficiency presented the same rate of psychomotor development as did non-anemic children, after four months of treatment with iron supplements.

Iron deficiency can also negatively affect cellular immunity, even before the child becomes anemia, and this can lead to an increase in illnesses such as diarrhoea, respiratory disease and other infections. These effects can be reduced by iron supplementation or good fortification.

Forms of control

Despite the efforts by the World Health Organization (WHO), with their disease eradication programmes, most of the world still faces difficulties in eliminating public health problems. In Brazil, the 8- National Health Conference, which took place in 1987, accepted the health depends, among other things, on the state of the diet, housing, environment, salary, transport, leisure, liberty and access to healthcare services. This stance diverts attention from the disease as presented to the doctor, and leads to consideration of the human being as a whole and his living conditions. Thus, the emphasis in the debate on health is redirected from the purely biomedical and curative viewpoint to a broader, preventive new involving social and educational aspects.

Additionally, the debate on health as a basic human right has been reopened. To this, a special emphasis on childrens' rights to health should be added, because of their immaturity and consequent incapacity for self-determination and defense, and emphasis on the responsibility of governments to guarantee and protect this right.

For breastfed babies and young infants between 6 and 24 months old, iron supplementation is the main form of treatment for iron-deficiency anaemia (with a prevalence of at least 20%)*. Other actions carry the implication of mid-term and long-term interventions, to be developed by health organizations, such as the fortification of cheap and easily available foods and the diversification of foods promoted by education programmes[7]. Suchstrategies need implementation urgently, especially for the six to 24-month age group.

Supplementation with ferrous sulfate, either intermittently or weekly, is one short-term strategy that can be applied in wide-reaching programmes, since it presents two advantages: diminishing the side-effects from ferrous salt ingestion and reducing the costs of daily utilization of the mineral. Food fortification should be utilized as a prophylactic measure, choosing specific foods regularly consumed by the population. Domestic drinking water has also been used for fortification purposes, giving good results in children.

Dietary guidance is a strategy that should be simultaneously implemented with some other type of programme, with the aim of improving the bioavailability of iron. In infants under 24 months of age, higher intake of iron originating from plants is observed, but this iron has lower bioavailability. Therefore, to improve iron absorption, meat ingestion should be encouraged because it is rich in bioavailable iron, and/or vitamin C should be included when the diet offers low bioavailable iron.

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Images in Medicine

Clinical photographs of a 55 yrs. Postmenopausal female, a known case of scleroderma treated for breast cancer. It is notable that imaging studies in the patient show features of interstitial lung disease difficult to differentiate from lymphangitis carcinomatosa. In the latter case more diffuse, nodular pattern with kerleys lines are more prominent.

Fig. 1 Photograph showing the typical puckering of mouth in scleroderma

Fig. 2 Photograph depicting sclerodactly (glistening, thickening, hide-bound telangiectatic skin), atrophy and beaking of nails (pseudoclubbing)

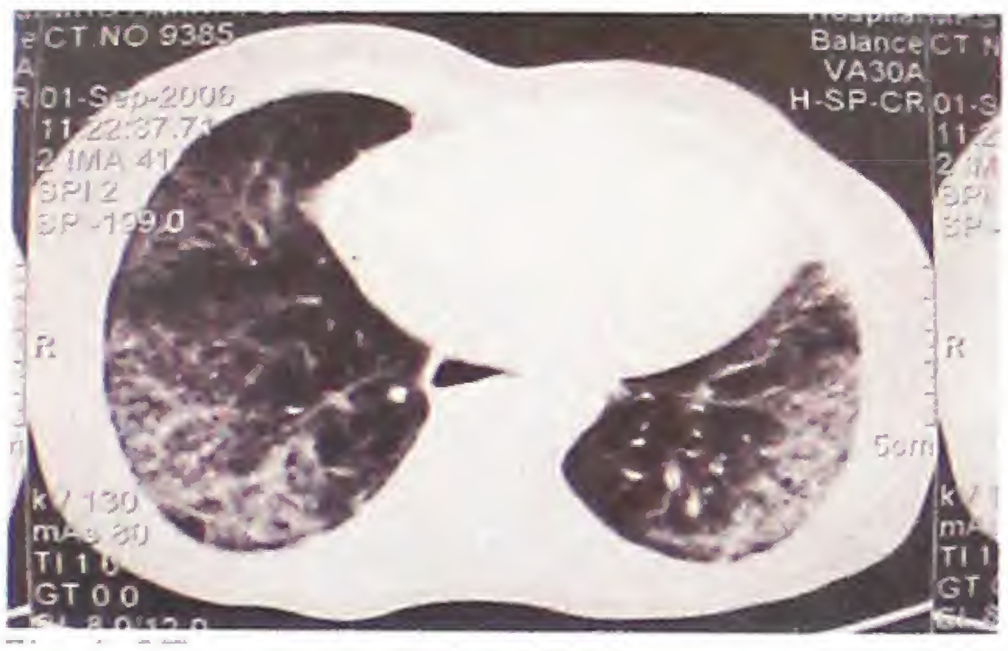

Fig. 3 CT Scan showing bilateral extensive interstitial fibrosis with cystic changes.

Fig. 4 X-ray chest showing interstitial disease pattern restricted to bases.

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Human Immuno Deficiency Virus (HIV) Infection & Role of Hospitals

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Abstract :

Human Immuno Deficiency Virus (HIV) infection a dreaded scourage has far reaching consequences on human lives. In a recent UN report it has been estimated that world has HIV infected population of about 40 million with almost half infected adults being women. Globally HIV is known to spread rapidly if it crosses 1% prevalence in the adult population. It is reported that in India about 5.1 million were living with HIV in 2003 and in states of Andhra Pradesh, Maharashtra, Karnataka and Nagaland, HIV prevalence has crossed the 1% mark among pregnant women. It has been also reported that the sex workers and drug injectors are topping among the high-risk group of patients in some Indian states. As per the estimates about 10% patients infected with HIV are expected to be seriously ill requiring hospital in patient care and about 30-40% with symptoms requiring care at the various ambulatory care facilities. Such a scenario puts among others, health care professional/ workers at a higher risk of exposure to HIV infection from the patients seeking help from the various health care institutions. In order avoid its consequent effects a multi disciplinary approach is required. The modern hospital, a complex of multi purpose institution has varied functions which include the prevention and treatment of diseases, the education of health professionals / workers and patients and conduct of bio-socio and clinical research based on the community needs. Thus hospital in tackling the problem of HIV/ AIDS need to have a policy statement focusing on the needs of HIV positive patients and on the specific risks of providing care to such patients. The hospital are to provide infrastructure, trained manpower, and required material and sound hospital practices that would facilitate prevention and control along with the treatment of the patient. Hospital will also be required to ensure safe blood/ blood products transfusion, undertake various information, education and communication activities regarding HIV risks, prevention strategy. The hospitals need to initiate a clear policy regarding use of various disposables, sterilization and sound disinfectant and antiseptics practices in the hospital settings. Without aggressive prevention efforts the menace of HIV/AIDS will continue to spread thus every health care professional / workers has a role in identifying people at high risk, offering education and counseling, encouraging testing and linking HIV positive patients with treatment and social service. This is the most cost effective humane way to reduce the ill effects caused by the HIV / AIDS disease and avoid a global disaster in the world especially in the South East Asia with India being no exception.

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Nosocomial Infection is the single most important factor that adversely affects the performance and image of the hospital. The greatest contribution to science has been to demonstrate, by sound laboratory and clinical research, a rational approach to understanding the causation of infection based on Pasteur's demonstration of an unseen ambient microbiological world. His revolutionary approach emphasized that microorganisms must be prevented from entering a wound during or after operation and that if microorganisms were already present, they must be prevented from spreading and Health Care Workers / Professional have a crucial role to play in this regard.

Hospital policy regarding AIDS should aid in fulfilling the basic objectives and responsibilities of the hospital. The modern hospital is a complex, multipurpose institution, its functions include:

- Ø The prevention and treatment of disease.
- Ø The education of health workers / professionals and patients.
- Ø The conduct of clinical research.

The most fundamental goal of the hospital is to benefit its patients. This goal is grounded responsibilities to provide competent and considerate health care and to protect patients from avoidable harm. In addition to patients, the hospital bears responsibility to the health care workers and employees who work within it from unnecessary risk of harm in the performance of their duties.

Implications of HIV for hospitals: The unknown, apparently healthy HIV infected is reporting to hospitals, clinics and other healthcare institutions for various medical, surgical, gynecological and other ailments, just like any

other patient. With the present estimated prevalence and keeping in view the patient load at different types of hospitals, the following scenario is expected: -

- Ø Medical school/ state level hospitals with Out Patient Department load of about 1000-2000 per day on an average of 1-2 asymptomatic / symptomatic HIV positive cases is being unknowingly treated every day.
- Ø District hospitals with Out Patient Department load of 3-4 hundred patients per day will have 1 or 2 seropositive patients per week.
- Ø Pregnant women: Statistical projections of HIV prevalence in pregnant women, suggest that on an average about 20,000 deliveries in seropositive women take place every year of whom about 6000 deliver HIV infected babies (33%); thus health care professionals would be conducting deliveries of HIV positive women.
- Ø This load, as per projections, is going to increase in the years to come, thus as a routine all hospitals, Primary Health Centers and other healthcare institutions need to implement infection control procedures all the time.

Risk factors for occupational HIV infections: The risk for occupational HIV was increased when:

- Ø The occupational exposure is deep as compared with superficial (P<0.0001)
- Ø Blood is visible on the device causing the occupational exposure (P=0.0014)
- Ø The device causing the exposure has been placed in a source patient's vein or artery (P=0.0028)
- Ø The patient dies within 60days of the exposure (P=0.0011)
- Ø The exposed health care worker does not take Zidovudine post exposure chemoprophylaxis (P=0.0026)

(Risk factors for occupational HIV infection identified in retrospective case control study in the USA, UK and France. (CDC and Prevention)

HIV infection is transmitted via blood, semen, and other body fluids; caring for HIV positive poses some risk to health care workers / professionals who come in contact with these body fluids. As the number of HIV positive patients grow the risk of exposure increases. Transmission of infection cannot occur, however, unless infected fluids have some route of entrance into the body, such as a needle prick, open wound, or mucous membrane exposure. Even when these exposures do occur, the risk of infection is very low. In a recent review of 5 published studies of a total of 770 HCP / HCW who accidentally received parenteral or mucous membrane exposure to infected body fluids, only 3 persons were HIV sero–positive and in only 1 of these cases, involving deep intramuscularly injection of a substantial quantity of blood was sero conversion documented by blood samples obtained before and after the event. This review concludes that the upper 95% confidence limit for the risk of infection after accidental exposure to HIV is 0.76% compared with a 12-17% risk of sero conversion after accidental injection of blood or serum from patients positive for Hepatitis B surface antigen.

Tuberculosis (TB) is the most common and most deadly infection for HIV +ve individuals. According to the CDC, people co-infected with HIV and TB are up to 800 times more likely to develop active TB disease during their lifetime than people who are HIV negative. TB is the cause of death for one of every three people with AIDS worldwide. Spread of HIV has helped fuel TB epidemic. The CDC recommended that all people infected with HIV should be tested for TB, and if infected, should complete treatment as soon as possible to prevent the onset of TB disease.

The CDC estimates that approximately one quarter of HIV positive people in the US are also infected with HCV. Incidence is even higher among HIV positive injection drug users (50-90%). The US public health service guidelines recommended that all HIV infected persons should be screened for HCV infection. The CDC also recommends that susceptible co-infection patients should receive Hepatitis A and Hepatitis B vaccines. Their risk of developing either or both of these viruses is increased by the co-infection. The risk of developing HIV infection from a needle prick with infected blood is about 1:300 without prompt antiretroviral treatment. To prevent transmission of HIV to Health Care Workers, the CDC recommends that post-exposure prophylaxis (PEP) should begin within 1-2 hours after the exposure (CDC 2001).

Care of HIV positive patients required exotic technology or professionals with special expertise unavailable at most hospitals, the care of such patients might be an unreasonable burden for most hospitals to bear. In fact, however such patients need hospital care for many conditions of all kinds, and the nature of that care is often not significantly different from that of other patients. Refusing hospital care on the basis of HIV infection or AIDS would be an unfair, callous, and unreasonable action. Such a refusal would be as unfair as refusing care solely on the basis of a patient's race, sex, or religion. Therefore, especially in view of the significant potential for discrimination against HIV positive patients, hospitals should clearly express their willingness to care for these patients.

Number of AIDS patients grows rapidly over the next few years, their exclusion from most low experience hospitals would greatly exacerbate the already serious burdens of AIDS care at high experience hospitals, threatening the survival of these latter hospitals and ultimately jeopardizing access to care for AIDS patients. Rather than turning away AIDS patients, then, hospitals with few AIDS patients should perhaps attempt to gain more experience in caring for them, or at least provide intensive education in the care of AIDS patients for their personnel. Bennett et al suggests that policy makers consider creating regional AIDS centers, which could be especially valuable in pursuing clinical research on AIDS.

On establishment of HIV infection in a community it is estimated that out of total infected patients 10% will be seriously ill requiring hospital in-patient care. 30-40 % will be symptomatic, requiring out patient care etc. with the present available hospital beds about 7 lakh bed in government sector (including ESI, PHC), there will be acute shortage of hospital beds even for AIDS related cases.

A public maternity hospital need not care for non-obstetric AIDS patients but should be willing to provide obstetrical care for women with AIDS who need such care. A private maternity hospital should also provide appropriate care for a woman with AIDS who can afford that care. Presently there is no law enacted to make it mandatory for private and missionary hospitals, to treat HIV positive cases, (although some private/ missionary hospitals on their own initiative have decided to accept HIV patients for treatment, just like any other patient). Further in view of chronic illness and cost many patients will not be able to afford private hospital treatment. Thereby HIV patients will use government hospitals in India.

HIV Virus, relevant to its transmission in Health care setting.

In view of the persistent, wide spread fear of contracting AIDS, hospitals must make a strong effort to educate and counsel their workers on the extent of their risk and on techniques for risk reduction. Better understanding of the situation can allay a great deal of fear and overcome reluctance to care for HIV positive patients. After providing appropriate education and counseling, therefore, hospitals should also take action against employees who refuse to take care for patients with the HIV infection.

- HIV is transmitted through blood and blood related body fluids / products (Serum, pus and blood fractions), and through semen and vaginal fluids. Infectious fluids also include other body fluids with the above infectious fluids such as bloody or purulent sputum, saliva, bloody feces, urine etc.
- HIV is not transmitted through Saliva, Urine, tears, sweat and feces (so long as these are not contaminated with infectious body fluids).
- Breast milk is a route of transmission particularly in a recently infected woman (mothers who were sero negative before delivery, but accidentally transfused HIV +ve blood during delivery).
- HIV is an extremely fragile virus, inactivated by drying within a few minutes on exposure to atmosphere.
- Relative infectivity and risks with HIV
    - *Exposure preventable.*
    - *Prevalence of patients increasing.*
    - *Virus titer 10 to 1000 per ml of blood.*
    - *Infection risk with single exposure < 1%.*
    - *Prevalence in HCP < 0.01 in USA.*
    - *Mortality rate > 90%.*

Still in spite of low infectivity less than 1% (HBV 10-13%) has succeeded in raising and unprecedented awareness of infection control, which HBV did not.

- HIV is readily inactivated by the most commonly available disinfectants and by routine infection control measures.
- Intact skin is a complete barrier against HIV. Risk of infection from needle injuries is less than 1%. Prolonged direct contact of blood or splashes of blood into open skin lesions, eyes, or mucous membrane of nose or mouth also carries risk of transmission (0.1%).
- HIV transmission through aerosol inhalation has not been documented so far. (Aerosol are not released into the atmosphere in the course of surgeries)
- Risk of transmission from HIV infected HCP/ HCW to patient does exist. HIV infected surgeons or any HCP should not be involved in invasive procedures.

Prevention strategies to decrease risk of HIV infection.

- Use of Standard Precautious or of other Isolation Procedures designed to place effective barriers between HCW/ HCP and blood or other body fluids.
- Educating new staff and retraining existing staff regarding occupational risks for blood-borne pathogen infection in the context of other occupational risks present and prevalent in the health care work place; making certain staff aware of these risks.
- Including information about all occupational risks in biomedical training schools curricula.
- Evaluating all procedures associated with occupational risk for exposure to blood borne pathogens (particularly those presenting risks for trans coetaneous exposure), with the intent at modifying the aspects of those procedures associated with risks for occupational exposures.
- Aggressive use of newly developed engineered controls, including careful evaluation of safety devices for safety, efficacy and cost-effectiveness; implementation of those devices that meet these tests.
- Development of efficient, readily accessible, user-friendly institutional post exposure management systems, including the option for post exposure antiretroviral chemoprophylaxis for documented occupational HIV exposures (Beekmann et al).

Infection Control Practices:

Hospital Infection control Practices can reduce the risk of exposure to HIV infected blood and body fluids. Center for Diseases Control (1987) has recommended the use of Barrier Precautious for all patients when contact with blood or body fluids is anticipated, this approach, usually referred to as "Universal Precautious", has been endorsed by the American Hospital Association (1987): Under universal precautions, HCP/HCW should assume that the blood and other body fluids from all patients are potentially infectious, and therefore should follow infection control precautious at all times and in all settings. Meticulous adherence to universal precautious is recommended by CDC for the care of all patients and mandated by Occupational Safety and Health Administration (OSHA). "Standard Precautious" is a newer term that hospitals and other agencies are moving towards. It includes all recommendations for Universal Precautious plus body substances isolation (BSI) when other potentially infectious material (OPIM) is present.

Universal Blood and Body Fluid Precautious/ Standard

Precaution:

- Hand Washing
- Barrier techniques to prevent contact of blood or body fluids with skin or mucous membrane includes
  - Use of gloves
  - Use of mask.
  - Protective eye and face shields, when appropriate.
  - Gowns and Aprons.
  - Compulsory use of fully buttoned up aprons in labs.
- Ban on mouth pipetting of blood / serum for tests.
- Disinfection of soiled material / used instruments / soiled surfaces.
- Hospital Waste Disposal.

Risk to HCW / HCP of HIV infection even after accidental parenteral exposure is low the risk to other patients from HIV +ve patients must be vanishly small since the exposure of patients to the body fluids of other patients in modern hospitals is rare and all but eliminated by prescribed infection control practices such as hand washing after patient contact. A potentially greater risks to non infected patients would be contact with HIV +ve HCW / HCP, though the degree of risk in this case presumably would depend on the nature of such contact and especially the potential for parenteral or mucous membrane exposure to body fluids of the infected HCP. Documented case of transmission of HIV infection from two HCP(a dentist and an orthopedic surgeon) to patient.

Hands of the hospital personnel are by far the most convenient vehicle for transmission of infection while the hands of the carrier are frequently used to comfort and treat the patients. The role of hands in cross infection is paramount. The modest measure of hand washing is to decontaminate hands off the transient organisms is most often ignored, resulting in vulnerability of the patient in the hospital to itrogenic nosocomial infection. The majority of transient organisms are removed by mechanical action of hand washing or chemical action of hand disinfection. Nevertheless HCP/ HCW fail to wash their hands and still fail to appreciate the importance of doing so.

Work practice controls can eliminate a substantial fraction of occupational exposures to blood-borne pathogens; modifying medical devices associated with exposure risks can reduce risk further. Some of these devices have been tailored to the needs of specific hospital settings (e.g. the operating suite); other specific procedures (e.g. phlebotomy) are associated with decreased risk of cutaneous and / or percutaneous blood exposures:

- A surgical repair assist device.
- Blunt surgical needles.
- Surgical finger guards and glove liners.
- Phlebotomy equipment.
- Needle-less intravenous administration systems.
- Modified (e.g. self-capping) intravenous catheters.

Developing a systematic approach to the assessment of new safety devices has been suggested, emphasizing the importance of creating a multidisciplinary team, including the primary users of the devices, to assist in:

- Performing the analysis;
- Developing prevention strategies tailored to an institution's specific needs;
- Developing relevant criteria for assessment of the design and performance of the device;
- Objective testing of the devices in clinical settings;
- Carefully analyzing performance and cost-effectiveness before making a product selection.

Development of a process for the systematic objective evaluation of these devices is crucial for effective risk reduction at all health care institutions.

Particular precautious during care of Sero Positive individuals:

- According to NACO, it is safer to care for HIV +ve patients in the general ward, provided sterilization and disinfection of invasive instruments/ equipments is being done. Gloves are not to be used for routine patient.
- Nurses/ HCW with cuts / injuries or dermatitis should have water proof dressing on it. Preferably they should not work with HIV patients as long as broken skin on hand, and forearm or other vulnerable areas are there.
- Storage and transport of items used on sero-positive cases should be separate, marked and kept in puncture resistant containers, containing appropriate disinfectant.
- All spillage/ contamination/ soilage of blood and body fluids should be flooded and soaked in 1% bleach solution for 30 minutes.
- Linen soiled with blood / OPIM be treated as contaminated. Contaminated laundry must be bagged at the location where it was used, and shall not be sorted or rinsed in patient care areas. It must be placed and transported in bags that are labeled or colour coded (red). Laundry workers must wear protective gloves.

The cotton and acrylic/ synthetic blanket are preferred to woolen blankets since these can be easily decontaminated when soiled and washing is also cheap and easy. These can be handled like linen. Contaminated soiled woolen blankets can be decontaminated either by exposing to formaldehyde vapours or autoclaving.

- All infectious waste must be placed in closable, leak proof containers or bags that are colour coded (red) to prevent leakage during handling, storage and transport, essentially decontamination and safely rendering unfit for reuse.
- Tags must be used until the identified hazard is eliminated or the hazardous operation is completed. Tags must contain a signal word or symbol and a major message. The signal word shall be "BIOHAZARD" or the biological hazard symbol. All employees are informed about the meaning of the various tags used throughout the

workplace and what special precautions are necessary.

- Electronic thermometers with disposable covers do not need to be cleaned between users unless visibly soiled. Glass thermometers should be soaked in 70-90% ethyl alcohol for 30 minutes, and then rinsed under a stream of warm water between each use. Glass thermometers pose an additional hazard because they contain mercury, which is a potent neurotoxin.

Special care during surgery of HIV patients:

- Reconsider the need for the surgery pros and cons, wound healing etc.
- Use of disposables as for as possible.
- All non-disposables including tubing's, suction fluid bottles, humidifiers used, to be thoroughly cleaned and disinfected, if not possible to clean exposed interiors, such items should be discarded after decontamination.
  - Knife preferred to diathermy.
  - Skin closed by clips, not sutures.
  - Thorough cleaning with 1% bleach of floor, walls, table sides, surgical light, fans, trolleys, every other possible place with 7% Lysol.
  - Use of protective Barriers.

What should be done following an exposure?

- Don't get panicky
- Needle pricks and cuts should be washed with soap and water.
- Splashed to the nose, mouth or skin should be flushed with water.
- Eyes should be irrigated with clean water, saline or sterile irrigates including contact lenses.
- Do not put the pricked finger in mouth reflexly.
- Report the exposure to concerned authority.
- Treat the condition as an emergency preferably within two hours.

Prevention & Risk reduction:

HIV/ AIDS are preventable. Screening of blood and blood products for the HIV has reduced the risk of HIV transmission with transfusion to 1:1,000,000. Following universal precautious in health care has unquestionably prevented thousands if not millions of cases of HIV/ AIDS. According to the CDC, occupational exposure to HIV has resulted in only 57 cases of HIV sero conversion among health care personnel in the U.S. between 1985 and June 2001. That's the good news. Virus is transmitted through behaviours that many people find pleasurable-sexual activity and injection drug use prevention can be difficult, but not impossible. "Stigma and discrimination are the major obstacles to effective HIV/ AIDS prevention and care. Fear of discrimination may prevent people from seeking treatment for AIDS or from acknowledging their HIV status publicly. People with, or suspected of having, HIV may be turned away from health care services, denied housing and employment, shunned by their friends and colleagues, turned down for insurance coverage or refused entry into foreign countries. In some cases they may be evicted from home by there families, divorced by their spouses, and suffer physical violence or even murder. The stigma attached to HIV/ AIDS may extend into the next generation, placing an emotional burden on children who may also be trying to cope with the death of their parents from AIDS. Focus on stigma and discrimination; campaign will encourage people to break the silence and the barriers to effective HIV/ AIDS prevention and care.

Action Plan

1) Develop a sound and effective hospital infectious control policy and monitor its implementation.
2) Health education to public/ patients and attendants.
3) Awareness programmes for the hospital staff including doctors, nurses and other health care workers.
4) Hospital staff to assume that every patient is potentially infectious.
5) Encourage use of Universal Precautions and Standard Isolation Precautions.
6) Develops an effective method of reporting exposure pricks/ cuts and implement the recommended protocol to handle exposed staff.
7) Earmark a specific inpatient area with facilities of barriers nursing for admitting the AIDS case with TB.
8) Logistics to be made available to the staff treating AIDS cases.
9) Safe and appropriate policy for hospital waste from generation to final disposal.

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Completeness of Blood Transfusion Forms in SMHS Hospital Srinagar

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Abstract :

In the study one thousand blood requisition forms from various departments of SMHS Hospital Srinagar were scrutnized to assess the completeness of information submitted about the patients requiring transfusion. It was found that complete patient address was mentioned only in 1.4% of patients, partially complete address in 67.5% of patients and no address was mentioned in 31% of patients. Provisional diagnosis of patients was mentioned in 60.2% patients, indication for transfusion was mentioned in only 56.6% of patients, history of previous transfusion in 59.8% patients. Indication for type of blood requisition in 69.2%. Relative donors were provided in 83.8% patients. Indication for transfusion given apparently coincided with provisional diagnosis given in 93%, type of requisition mentioned apparently coincided with clinical diagnosis given in 84% of cases.

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INTRODUCTION

Blood transfusion is an essential component of therapy for a wide variety of disorders. Until Harvey's doctrine of the circulation of blood was proposed in 1616, the concept of blood transfusion had no rationale. The concept of transfusion therapy developed once it had been accepted that blood circulated and that the intravascular space might be replenished with fluids introduced from outside the body. The first transfusion of blood in humans occured in 1667[1]. Progress was slow thereafter because of the complexities of transfusion, which we now recognize, particularly the incompatibility of interspecies and intra-species transfusion[2]. By the early 20th century, transfusion as a therapeutic measure was still cumbersome and risky, but during and shortly after world war I, technical progress permitted the rapid expansion of blood banking and of blood transfusion as a therapeutic modality.[3].

Recently component therapy has broadened the application of transfusion therapy from blood volume support to the specific replacement of most blood cells and many plasma proteins. However, prudent use of these agents requires an understanding of their indications, limitations, potential benefits and hazards[4-9]. Technical advances continue, particularly in the more efficiently use of components and fractions of donor blood, improvement of donor screening techniques, immunological matching of donor blood products with recipients and development of recombinant products. Transfusion medicine has recently been recognized as a specially of its own. The Acquired Immune Deficiency Syndrome epidemic and transfusion of other infectious agents through blood transfusion have revolutionized the practice of transfusion medicine. A detailed information regarding the blood group, history of previous transfusions, antigen/antibody status of the recipient is essential to ensure safe transfusions. Similarly the detailed documentation of the various tests done on the donor blood is essential to trace out any source of error which may be responsible for the minor or the major transfusion reaction. We undertook this retrospective study to study the completeness of the documentation regarding blood recipient (clinicians job) and regarding issued donor blood (Blood Bank Job).

MATERIALS AND METHODS :

The study titled "Completeness of Blood requisition Forms in

SMHS Hospital Srinagar" was carried out in the Transfusion Medicine & Hematology Department of SMHS Hospital Srinagar. One thousand Blood requisition forms received for blood transfusion from various departments of SMHS Hospital Srinagar like Surgery, Medicine, ENT etc. over a period of six months were included in the study. All the requistion forms were scrutinized and analyzed as per the following proforma.

OBSERVATIONS & DISCUSSION:

The study of completeness of Blood requisition forms in SMHS Hospital Srinagar was carried out with a view to assess the seriousness of resident staff in various departments of SMHS Hospital Srinagar in filling the various columns of Blood Requisition Form which are purely essential and scientific.

1.	Patients address	Complete / Partly Complete / Not given
2.	Diag / Provisional Diagnosis of Patients	Mentioned / Not mentioned
3.	Indication of Transfusions	Mentioned / Not mentioned
4.	Whether indication for transfusion given coincides with clinical diagnosis	Yes/Not
5.	History of previous transfusion	Mentioned / Not mentioned
6.	Type of requisition (Stat / Routine / Urgent)	Mentioned / Not mentioned
7.	Whether type requisition mentioned coincides with Clinical Diagnosis	Yes / No
8.	Relative Donor Provided	Yes / No
9.	Reasons for not providing relative donor	Given / not given
10.	Blood Receipt by treating Unit	Complete / Incomplete

Blood centers are licensed in accordance with the manufacturering guidelines of the Food and Drug Administration (FDA) in the United States or its counterparts in other countries. Additional professional standards are set by the American Association of Blood Banks (AAB)[4] in USA. In India Blood transfusion practices have become safer after the Supreme Court ruling and after the implementation of decisions of drug and cosmetic act of India. Accordingly complete patient and donor information is not only essential but is also scientific. In our study residential address like District, Tehsil, Village / Mohalla was mentioned in only 14 (1.4%) requisition forms. 676 (67.6%) forms had incomplete residential address while as address was not mentioned at all in 310 (31%) requisition forms. Diagnosis/Provisional diagnosis of the patient needing transfusion was mentioned on 602 (60.2%) requisition, while in 398 (39.8%) requisition forms it was not mentioned. Indication for blood transfusion was stated in 566 (56.6%) requisition forms while as it was stated in 434 (43.4%) requisition forms. Indication for transfusion given apparently coincided with the diagnosis/provisional diagnosis given in 526 (92.93%) patients while it did not apparently coincide in 40 (7.03%) patients. History of previous transfusion about the patients in need of blood was mentioned in 598 (59.8%) patients and it was not mentioned in 402 (40.2%). Type of blood requisition weather urgent, routine, stat etc. was mentioned in 692 (69.2%) requisition forms and it was not mentioned in 308 (30.8%). It apparently coincided with a mentioned provisional diagnosis in 580 (83.81%) patients and did not apparently coincide in 162 (16.2%) patients.

Donor selection is undertaken with two goals in mind, to protect the health of the donor by ensuring that a donation does not place the donor at risk, and to protect the recipient by ensuring that the donor meets all health and screening criteria so that the risk of transmitting infectious agents or causing other adverse events is minimized [4,8,10]. In our study voluntary donors were provided in 838 (83.8%) patients while as 162 (16.2%) received free blood from unpaid volunteers. The paying of donors for fresh blood products for transfusion was discontinued after studies in early 1970s demonstrated that paid donors had a substantially higher prevalence of Hepatitis [11,13]. In our study patients who received free blood were mostly Bullet and Blast injury patients, or patients with no attendant, or patients with attendants who had already donated. Blood receipt by the treating unit was complete in 892 (89.2%) requisition forms while as it was partially complete or incomplete in 108 (10.8%) requisition forms.

It is concluded that the resident staff of the hospital do not take the documentation of the records very seriously. We have to make efforts to train residents in this direction. The senior faculty staff of the hospital has to ensure that the resident staff is taught about the essentiality of proper documentation. The Blood bank staff may not accept incomplete forms in routine cases.

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SOCIAL CLASS & HEALTH STATUS

Syed Amin Tabish,

Social class affects one's life chances across a broad spectrum of social phenomenon from health care, to educationa attainment, to participation in the political process, to contact with the criminal justice system. Health inequalities are a endemic characteristic of all modern industrial societies, but the size of the differential varies between countries and ove time, indicating that there is nothing fixed or inevitable about having such a health divide. Inequalities in health ar differences that are unnecessary and avoidable and judged to be unjust and unfair. Inequality in health is mainly consequence of large economic and social inequalities in society. However, sound health policies can reduce inequalities eve in the face of income inequality. Observed social inequalities in health are amenable to purposeful policy interventions. determined effort to mobilize the political will to create a fairer society that embraces all sections of the community is urgentl needed.

Inequalities in health are differences that are unnecessary and avoidable and judged to be unjust and unfair. Inequalities are restrictions of choice of lifestyle, exposure to unhealthy living and working conditions and inadequate access to essential health and other public health services. Equity, is therefore, concerned with creating more equal opportunities for health and reducing differentials to the minimum. The inequalities include differences between geographical areas both within and between countries, ethnic groups in the population, occupations which can be classified into social classes, those with jobs and those who are unemployed, those with different levels of educational achievement, income groups, and the sexes.

It has been estimated that in the average developing country the top 10 percent of the households receive 40 per cent of income and the bottom 40 per cent receive 10 per cent of the income. Extreme poverty is very damaging to health particularly through malnutrition. Poor nourishment reduces resistance to disease. Malnourishment leads to both poor physical development and poor mental development. The underfed child is less able to absorb education.

One of the most persistent disease patterns observed in public health research is that people in lowest socio-economic groups have the highest rates of morbidity and mortality. This differential has been observed throughout the world, regardless of whether the dominant disease of death and disability were attributed to infectious or non-infectious causes and regardless of the specific methods used to assess socioeconomic status.

A more appropriate social epidemiology would take advantage of current discrepancies and inconsistencies in the research evidence by developing better research methods and instruments, by thinking about more appropriate disease classification systems, by exploring more precisely the ways in which psychological factors affect immune function, by considering more systematically the possibility that what happens early in life, and by moving beyond models that do not consider disease pathways beyond those of an individual.

The importance of social factors in the etiology of many diseases is becoming increasingly clear. It is impressive that an increasingly large body of consistent findings is being generated in spite of these major methodological problems. Intervention in the social environment clearly is necessary, and continued research on social factors therefore must become an important priority in both public health planning and programme development.

One of the causes of the inequalities is that lower social classes are unlikely to use preventive services. Higher social class receives more explanations of their health problems as compared to lower social classes. In addition, for any sickness, the higher social classes are more likely to go to a doctor. The health services do not actually succeed in providing equal access for equal need as intended.

Health inequalities are an endemic characteristic of all modern industrial societies, but the size of the differential varies between countries and over time, indicating that there is nothing fixed or inevitable about having such a health divide.

Social Stratification

Social stratification refers to the division of a society into layers (strata) whose occupants have unequal access to social opportunities and rewards. People in the top strata enjoy privileges that are not available to other members of society, people in the bottom strata endure penalties that other members of society escape. The upper class consists of relatively few individuals (1 percent of total population) with great wealth and great power in the economy. Upper middle class (10 percent of total population) consists of successful business people, executives, professionals, and high ranking civil and military officials. The lower middle class (30 percent of total population) also consists of professionals and small business people. The working class (40 percent of total population) consists of skilled and unskilled (blue collar) workers. Lower class (20 percent of total population) consists of the poor. The under class constitute 1 percent of the population. In a stratified society, inequality is the part of the social structure and passes from one generation to the next.

Factors influencing health

There are many Influences on an individual's health, often categorized into biological factors; the physical and

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social environment; personal life style; and health services.

Most influences on health demonstrate a social gradient, with conditions conducive to health becoming less favourable with declining social status. There is therefore an uneven distribution of health hazards and risk factors across the population, resulting in groups with lower status, power or income carrying a heavier burden of ill health.

National profiles of health and disease indicate the vast inequalities in health status that exist in many countries the underprivileged form part of every country's population. The international evidence on inequalities in health is compelling. People who live in disadvantage circumstances have more illnesses, greater distress, more disability and shorter lives than those who are more affluent.

In most developing countries, registration of births and deaths is seriously incomplete and, in some, considerable proportion of the population cannot state their age with any accuracy. Local surveys can, however, be used to estimate infant mortality rates.

Second, accurate data on income is difficult to collect as a high proportion of the working population works in the informal sector. But it is often possible to make comparisons between poorer and richer areas or between ethnic groups. According to World Bank report of 1993, in Indonesia, India and Kenya, child mortality is higher in states with higher proportion of poor people; within cities, there are large differences in child mortality rates between rich and poor neighborhoods.

An association between poverty and ill health has been recognized. It seems likely that cumulative lifetime exposure to health damaging or health promoting physical and social environments is the main explanation for observed variations in health and life expectancy, with health related social mobility, health damaging or promoting behaviors, use of health services, and genetic or biological factors also contributing. People with poor health move down the social scale and people with good health move up the social scale. There remain explanations of health inequalities in terms of behaviour and explanation in terms of material circumstances, though they are closely associated. The role of genetics (heredity) and environment are very important considerations of differential of longevity.

There are vast differences in health status between developed and developing countries. The high child mortality and the high death rate among the very young in developing countries results from diseases that have almost disappeared in developed economies.

Infants born in rural areas have a much lower chance of survival than urban infants do. The most vulnerable are farmers with inadequate resources, landless agricultural labourers with limited employment opportunities, the illiterate and the urban poor living in slums and shantytowns.

Damaging health behaviors are social class correlated but those that are known seem to explain much less than half of the social class variations and some lifestyles are strongly influenced by the social environment. Excess inequality is not just unfair but is in addition health damaging. Societies, which have less inequality in income, less variations in hosing, standards and better working conditions, seem to have less health inequalities between socio-economic groups.

People may be landless, members of minority ethnic groups, disadvantaged because they are old, sick, homeless, jobless, or inhabitants of remote marginal areas, or displaced persons. Most of the underprivileged in health terms are women and children whose well-being requires special attention within primary health care. The elderly are also vulnerable in many countries. Particularly in developing countries, these underprivileged elements of society are politically weak and are often too sick, illiterate, or geographically dispersed to become politically active. Thus, the responsibility for improving prospects for these groups will fall upon the more privileged groups. Concern for the care, protection and promotion of health of the vulnerable and underprivileged groups must be the task of governments, which have, after all, the responsibility for ensuring an equitable distribution of society's resources based on the principles of social justice. Disadvantaged people not only suffer from poor health but receive poor health care. Conversely, wealthy people enjoy not only better health but better access to health-related facilities. Development strategies that are compatible with the primary health care approach contrast with single-purpose quests for economic growth regardless of the human consequences. Strategies that promote economic growth and reductions in social inequalities and increase in social services are consonant with the goal of health for all. Government money alone will not guarantee achieving this objective. Political commitment and support are also critical

Lifestyle and health promotion

Lifestyle is the way of life, which is within the choice of the individual; however the limited range of choice may be. Changing lifestyle might seem to be the easiest and cheapest way of securing health improvement in a society at any level of development. If people learned to boil their water, bury their feces and household waste and select or grow the most nutritious diet, which is within their means, health status would show a notable improvement. If people did not smoke, take alcohol in access, were safety conscious on the roads and at work, a large amount of morbidity and mortality could be avoided.

Largely people are the prisoners of their values and the values of their society they live in, and are limited by their economic and social environment quite apart from any health knowledge they may possess. An authoritarian society may be able to some extent impose health on people whether they like it or not. But in most societies this would be unacceptable, except in very limited contexts. It is imperative to understand the different and often

conflicting pressures to which different groups of people are subject.

The deciding influences on behaviour are often social pressures – what the peer group does.

Social pressures are often strong enough to resist economic pressures. It costs money to smoke and drink but it is a price that has to be paid to participate in social life. Alternatively, economic pressures may reinforce social pressures. Healthy foods are not only more expensive but they also take longer to prepare. For those in low-income groups, time as well as money costs can be important determinants of behaviour.

Most people are highly responsive to social pressures, but not all. The value of planning is to be found more with those with better education. The completely educational process of climbing the ladder by passing a series of examinations require a willingness to sacrifice the present for the future. Not all are willing to do this. A job is seen as better than continuing as a student with the dependency on parents that this implies. If people have never absorbed middle class aspiring values, it is useless to direct health education messages at them as if they had. If life is a matter of luck and the future can take care of itself, it is of little interest to be told what activities, which give pleasure today, run risks of major health damage in the future.

The better educated are better served by the media. It has been found that the 'quality' press publishes more articles on health; is more informative by citing books, articles and government reports; and give more coverage of social factors in ill health such as unemployment and class inequalities.

Values, beliefs and social pressures can and do change over time, though the process by which they do may not be readily understood. Social pressures are certainly changing in Europe and North America. Smokers now usually have to ask permission to smoke. In developing countries, smoking rates are increasing in both men and women. The smoking habits of parents influence their children. While smoking has been on decline in Europe and North America, the producers have been concentrating for declining markets by putting their major efforts elsewhere.

Carefully designed and properly communicated messages (health education) can be used to promote health. Face-to-face contact between health professionals and the public is one effective way of changing behaviour. Giving people knowledge about what is favourable or unfavorable to health is far from being enough to influence health behaviour. Any attempt to improve lifestyle must be based on the choices that people in difficult circumstances can make, so that realistic, credible advice and help can be given.

A vital age group for health promotion is children aged 8 to 13. Health education should be comprehensive, should be continued over the years with a substantial time commitment and the same themes should be repeated at different stages of the course. The training of the teachers is critical and the involvement of parents highly desirable. This will help children to clarify their ideas, values and attitudes.

Vigorous action by government would help. If people were led to recapture their responsibility for their own health, the response to change in lifestyles would be better.

There is need to concentrate action in areas or districts with the lowest agricultural production per household, the poorest rates of school attendance, the highest indicators of malnutrition, or living in the worst slums. Special efforts can be made to improve take-up rates for immunization and other preventive care, and to improve the accessibility and quality of health services. Extra health education in schools and school meals can be provided in deprived areas and efforts made to improve sub-standard housing and reduce pollution. Population stabilization is essential.

Attempt to coordinate health policy at both the national and local levels, and developing community participation in action will go a long way to promote health of the nation.

Tackling Inequalities in Health

Strategies to tackle inequalities should focus on strengthening individuals; strengthening communities, improving access to essential facilities and services, and encouraging macroeconomic and cultural change. The aim of strengthening individuals has been to make up perceived deficiencies in knowledge, practical competence or stress management among people experiencing disadvantage, and to encourage the acquisition of personal or social skills to change their way of life or to be more resilient in the face of adversity. These policies see the problem they seek to address mainly in terms of an individuals personal education and development.

Interventions with a behavioural focus stand more chance of success if information giving is supplemented with personal support or structural changes that help make the behavioural change easier, and if the advice given is sensitive to the difficult circumstances in which many people live.

Community development is essentially about increasing the ability of marginalized communities to work together to identify and take action on priorities defined as important by the communities themselves. If people in marginalized communities were working well collectively they could influence their local environment in small but constructive ways: attracting resources to the area to improve housing and safety, for example, or working together to tackle crime or to limit substance abuse, or any other of their chosen priorities. These could lead to improvement in both physical and mental health in specific areas in the long run.

Community regeneration strategies focus on multiply deprived areas with typically about 10 to 20 thousand residents. They attempt to improve the social conditions in a neighborhood at the same time as stimulating the local economy to provide more employment opportunities and tackling defects in the physical environment. The aim is to achieve sustainable and, long-term improvements, acknowledging that three aspects – physical environment, economic opportunities and social conditions in a neighborhood – are all interrelated and therefore a coordinated

approach is essential.

Empowering communities by strengthening the rights of all citizens, including entitlement to services and accessible complaints procedures, could play a useful part.

Improvements in day-to-day living and working conditions and access to services have been shown to be beneficial for the health of populations. Initiatives include some of the classic public health measures to improve access to adequate housing, sanitation, uncontaminated food supplies, safer workplaces and health and welfare services. Such measures have the potential to benefit the health of the population in general, but especially that of the people living in the worst conditions, bringing about a reduction in the health gap.

The factors and policies that have, been influential in bringing about the striking improvements in health in developed economies resulting in the reduction in the risk of, or fatality from, infection as the main factor in the decline in mortality, brought about by the rise in the living standards, certain agricultural developments and extensive public health measures include improvement in nutrition, smaller family size due to fertility control, better provision of water uncontaminated with faeces, increased education and the application of scientific knowledge (control of communicable diseases, immunization, etc.) and to undo the negative effects of industrialization , such as improvements in dangerous and debilitating working conditions and the appalling housing conditions caused by rapid urbanization.

The World Bank suggests that governments must do more to promote a healthier environment, especially for the poor, who face greatly increased health risks from poor sanitation, inefficient and unsafe water supplies, poor personal and food hygiene, inadequate garbage disposal, indoor air pollution, and crowded and inferior housing. Collectively these risks are associated with 30 percent of the global burden of disease. Such public health measures are as important today as ever.

The impact on health of such provision (like improving water supply and sanitation) is significant in developing countries. Reduction in child mortality and disease severity are substantial. Programmes like *Head Start* in the USA and Canada,, targeting resources at the start on half a million children in the poorest countries, subsequently extended to 450,000 children was designated to be a comprehensive package of services providing early education at a day centre, immunization, medical checkups to detect hearing and vision defects, hot meals during the day, and social services and parental education/support for the families of children.. Controlled studies have found consistently positive results for the better-quality, more comprehensive schemes.

Countries that have implemented economic policies that have reduced poverty and brought about a more equal distribution of resources have made most progress in certain key aspects of health, such as life expectancy and infant mortality.

In developing nations advances in income and education have allowed households almost everywhere to improve their health. Macroeconomic policies that increased income was seen to work by increasing the ability of the people to obtain the prerequisites for health – food, housing, safe water, warmth, satisfying employment, etc. the importance of policies to influence the distribution of resources within a country is recognized, base on examination of policy in countries and regions that have achieved better health status than expected from their economic position. Rich countries like Japan and poor countries such as China, Costa Rica and Sri Lanka have all made impressive improvements in life expectancy and infant mortality, which appear to be associated with the more equal distribution of income that accompanied economic growth in these countries.

The impact of macroeconomic policies on the health of the most vulnerable groups in society therefore needs to be monitored carefully. Poverty reduction policies are potentially essential for tackling inequalities in health and, these would entail both ameliorating the effects of hardship through adequate social security provision for those who fall into poverty, and attempts to prevent poverty in the long-term.

A Strategic Approach

The importance of having a coordinated intersectoral strategy can be well illustrated in relation to community regeneration programmes for multiply deprived neighborhoods. Improvements in the physical fabric, which do not address underlying economic problems, are short-lived. Training and capacity building which is not linked into realistic opportunities for jobs or additional responsibility will not be seen to be relevant.

Action to tackle variations in health must be central to achievement of the government's national health policy. Everyone should have the opportunity to attain their full potential for health. Equity in access to and use of health services is a common goal for all. Equity is increasingly becoming an important issue especially when attention is focused on efficiency considerations. Health sector reforms are taking place in many countries globally. These will have serious implications if proper attention is not given to the poor, marginalized and vulnerable groups. Evidence from Sri Lanka and Malaysia indicate that provision of basic health services has indeed been an important mechanism for mitigating the impact of poverty in rural areas.

Health promotion activities are actively encouraged in most countries. Many healthcare providers and health experts are becoming increasingly concerned about the growing evidence of significant health inequalities between social groups, and in particular the strong association between relative deprivation and poor health. The Ministry of Health can play a key role in coordinating and implementing public health programs intended to reduce inequalities in health.

As part of the process for developing a health policy consistent with the economic policy embedded in 'Growth with Equity', and thus based on achieving equity in health, the government of Zimbabwe undertook a review of the

health sector. It adopted a policy to achieve equity in health. The policy emphasized the primary health care approach, broadening the social base of health activities and restructuring the health services from the base upwards. The policy also stressed the need for coherence between development and health policies and included as a priority for the government the strengthening of its institutional mechanisms for integrating development and health planning and for coordinating the work of the agencies responsible for health-related sectors, notably: health care, water supply and sanitation, local government and housing, rural development, agriculture, community development and women's affairs, and education.

Good health is the product of very complex range of factors, most of which are completely outside the control of health sector. Policies designed to equalize access to acute health care services would not have a substantial impact in reducing inequalities unless it is associated with task of changing the unhealthy behaviors of those living in deprived circumstances, or preventive measures of unproven effectiveness.

Policy initiatives

Policy initiatives that can influence inequalities in health exists at four different levels: strengthening individuals; strengthening communities; improving access to essential facilities and services; and encouraging macroeconomic and cultural change.

Policies that attempt to strengthen individuals aim to change people's behaviour or copying skills through personal education and/or empowerment. General health education messages have a limited impact on people from disadvantaged environments because the pressures of their lives constrain the scope for behavioural change. However, more sensitive interventions that combine education and support can have a positive effect on the health of people in disadvantaged circumstances if they are carefully tailored to their needs and combined with action at other policy levels.

Policies that aim to strengthen communities have either focused on strengthening their social networks or they have adopted a broader strategy that develops the physical, economical and social structures of an area. Such initiatives can, through involving the community itself in the determination of priorities, change the local environment, services and support systems in ways that promote equity in health.

Despite some successes, however, efforts to strengthen individuals and communities have had a minimal impact or reducing inequalities in health. Much greater influence is possible at the other policy levels. Some of the greatest gains in health in the past have resulted from improvements in living and working conditions – better housing, improved water supply and sanitation, safer conditions in the workplace, education, the alleviation of poverty and general provision of health and welfare services.

Macroeconomic and cultural changes are also important determinants of health because they influence the overall standard of living in a country and its distribution; attitudes to women, minority groups and older people; and major environmental factors such as international pollution. Policies at this level have been shown to have different effects on the various groups in society, creating major implication for tackling inequalities in health.

A Holistic Approach

The more the determinants of health are recognized and understood the more inescapable is the conclusion that a person's health cannot be divorced from the social and economic environment in which they live. Factors that increasingly recognized to be of critical importance and that shaped the thinking include the physical environment, such and the adequacy of housing, working conditions and pollution; social and economic influences such as income and wealth, levels of unemployment, and the quality of social relationships and social support; barriers to adopting a healthier personal lifestyle; and access to appropriate and effective health and social services.

The best way of reducing family poverty is to tackle its causes by ensuring that all people who wish to be economically active have access to well paid jobs. Useful steps in this direction would include better training opportunities and improved childcare facilities, as discussed below. However, the social security system also needs to be reformed.

Increasing child benefit would be one way of improving family income. However, a large investment would only result in modest increases in the income of poor families. A more cost-effective way of reducing family would be increase means-tested benefits such as income support and family credit. Other policies that would reduce some of the pressures on people with low income should include tackling problems of low uptake of benefits; replacing the social fund loans scheme with a grants system; ensuring that all households have access to vital utilities – such as heat, light and water – without the threat of disconnection. Not only might these measures reduce inequalities in health but they would also raise the resources necessary to finance a comprehensive strategy to promote social justice and equity in health.

A crucial step in tackling inequalities is the need to create opportunities for prosperous and fulfilling employment for all citizens. The causal link that runs from deprivation from poor schooling, unemployment, low earnings and poor health must be broken. Preschool education should be expanded, particularly children living in disadvantaged circumstances, to give them a better start in life and to create greater equality of educational

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Unravelling the psychological shadows of epilepsy

In the recent years, apart from the effective therapeutic management of epilepsy, the cognitive and psychiatric impact of the illness and various medications used to treat it are to be taken primary care of. This role requires a strong primary psychiatric background that enables the psychiatrist to understand the psychosocial impact that epilepsy, a chronic illness, can have and how epilepsy related cognitive deficits may affect patient's educational and employment opportunities and hence their sense of control and independence.

To abolish this disease, one must apply the element which is Opposed to it, and not what is favorable and habituated

On the Sacred Disease - Hippocrates

The psychiatrist may need to consult with the patient about disturbed relationship that may develop with in the family or spouses as a result of dependent positions in which many patients find themselves.

Another responsibility of the psychiatrist is to identify any primary or secondary psychiatric disorders that patients may have, such as personality disorders or disorders of affect or mood. Some of these disturbances may require additional medical treatment, and the psychiatrist needs to know how various psychotropic medications may interact with anti epilepsy medications. So, an understanding of psychiatric and social issues in epileptics and effective intervention along with the anti epileptic drugs is required for a full-fledged therapeutic measure, which is now widely practiced in western countries.

PSYCHIATRIC ISSUES

Epilepsy is associated with focal or regional cerebral abnormalities. Though local, these may impair functions at a distance and they can create a deleterious effect on the functional organization of the brain. Impairment of cerebral function may also impair the individual's ordinary mechanisms of psychological defense. These mechanisms, such as denial or projection, are the means by which an individual copes with the world[21].

Behavioral disorders:

Clinically postictal changes are well documented, ranging from localized Todd's paralysis[10] to profound global dysfunction following a generalized convulsion.

In some patients, postictal behaviour can involve complicated actions, such as reactive automatisms that follow complex partial seizures and may result in inappropriate semi directed responses, such as aggression towards some one attempting restraint. Other patients experience postictal psychosis[4].

Certain types of epileptic seizures cause chronic disruption in sleep organization, particularly a reduction in REM sleep [22]. It is well known that REM sleep deprivation can produce behavioral disturbance, including psychosis, so the possibility that this may be an indirect means by which some forms of epilepsy produce lasting interictal disturbances in behaviour needs to be further investigated.

Another potential source of epilepsy induced interictal behaviour problems would include the effects of chronic epileptic seizure on endocrine function[15]. Seizures are associated with release of Prolactin and other hormones, altering diurnal fluctuations and absolute levels in brain and blood, which could have dramatic effects on behaviour and might, for instance, account for the sexual dysfunction seen in some patients with epilepsy.

Learning disorders:

It can be seen that there is a close association between seizure disorders and learning disability. The history of epilepsy is particularly frequent in those with more severe learning disability, usually starting in childhood, and there are important associations with particular syndromes associated with learning disability.

Epidemiology of learning disabilities and epilepsy

Author	Prevalence of epilepsy/1000	Freq. of learning disability
Koul et al (16)	2.5	22.9%
Bharucha et al (3)	3.6	18.2%

(Includes cerebral palsy)

Personality disorders:

Although some patients show features of the Geschwind syndrome, (consistent pattern of personality change, associated with temporal lobe epilepsy) nature and number of behaviors appear inconsistent.

Changes in personality, behavior, and affect based on review by Bear[2]

1. Emotionality
2. Manic tendencies
3. Depression
4. Humourlessness
5. Altered sexuality
6. Anger, hostility
7. Aggression
8. Religiosity
9. Nascent philosophical interest
10. Augmented sense of personal destiny
11. Dependence, passivity
12. Paranoia
13. Moralism
14. Guilt
15. Obsessionalism
16. Circumstantiality
17. Viscosity
18. Hypergraphia

Psychosis of epilepsy:

Most postictal psychoses are precipitated by series of generalized tonie clonic seizures. More rarely, psychoses occur after single grand mall seizures or following series of complex partial seizures. Postictal psychoses account for approximately 25% of psychoses in epilepsy[7]. Inter ictal psychoses are less frequent and account for 10-30% of cases[7].

Affective disorders:

Chronic epilepsy is frequently associated not only with a characteristic broad range of affective symptoms as are typical for depressive disorders but also with anxiety, specific fears, and with distinctive symptoms of

Clinical characteristics of psychoses in relation to seizure activity

	Ictal psychosis	Postictal psychosis	Paricta psychosis	Alternative psychosis	Interictal psychosis
Consciousness	Impaired	Impaired or normal	Impaired	Noremal	Normal
Duration	Hours to days	Days to weeks	Days to weeks	Days to weeks	Months
EEG	Status epilepticus	Increased epileptic and slow activity	Increased epileptic and slow activity	Normalized	Unchanged
Treatment	Antiepileptic drugs iv	Spontaneous recovery in many cases	Improvement of seizure control	Reduction of antiepileptic drugs	neuroleptics

Adapted from the Comprehensive Textbook of Epilepsy Volume II Pg-2074

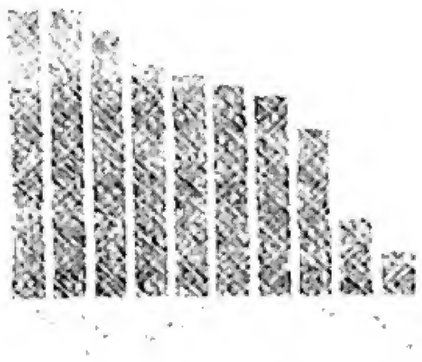
irritability and subtle brief euphoric moods.

Risk factors associated with interictal psychoses of epilepsy[4]

Sex	Bias to female patients
Age of onset	Early adolescence
Interval	onset of seizure-onset of psychosis: mean 14 years
Epileptic syndrome	Temporal lobe epilepsy
Seizure type	Complex focal
Seizure frequency	Low, diminished
Neurological findings	Sinistrality
Pathology	Gangliogliomas, hamartomas
EEG	Mediobasal focus, especially left sided

Adapted from the Comprehensive Textbook of Epilepsy Volume II Pg-2075

Key symptoms among 33 patients with interictal mood disorder[5]



Child psychiatric disorders in epilepsy:

Children with epilepsy are at risk for certain specific diagnosis. Symptoms of attention deficit/hyperactivity disorder have been found in approximately a third of the children with epilepsy. These children more often have symptoms of inattention than hyperactivity or impulsivity[8]

Mood disorders are also common, with approximately one fourth of adolescents with epilepsy having symptoms of depression[9].

Anxiety has not been assessed as often as mood disturbance, although two studies have found an increased risk, especially adolescents[11,18].

Approximately a third of children with autistic disorder may have seizures during their life time. The rare Landau – Kleffner syndrome of acquired epileptic aphasia is part of the differential diagnosis of autistic disorder. A schizophreniform psychosis has been seen in adults with epilepsy but seems to be uncommon in children, although Caplan et al. 1997[6] has found illogical thinking in children with partial complex seizures.

Suicide in people with epilepsy:

Gowers[12] was one of the first to document a specific relationship between suicide and epilepsy when he stated that "suicide although not a certainty is often a probable indication of a morbid family tendency, and some weight must be given to it as an indication of a disposition to disease of which epilepsy may be the result even when it has an immediate exciting cause". There is a general consensus that the risk of suicide in people with epilepsy is higher than that in the general population. Some studies suggest that the rate of suicide in people with epilepsy is around 4-5 times that of the general population and that those with TLE have an even greater risk (25 times and higher).

Suicide in people with epilepsy:

References	Deaths (n)	Suicides (n)	Deaths by suicide (%)
Prudhomme	1100	8	0.7
White et al	636	21	3
Freytag and Lindenberg	294	9	3.1

Adapted from the Comprehensive Textbook of Epilepsy Volume II Pg-2143

Other Psychiatric issues in epilepsy:

Panic attacks – although panic disorder can occur independent of epilepsy (due to temporal lobe dysfunction), the relationship between epilepsy and panic disorder is still considered to be a complex one. Anxiety states leading to panic attacks may develop out of the stresses of living with epilepsy, and they are reported to occur more often in those with epilepsy than in the general population.

Obsessive compulsive disorder (OCD) - there is occasional reports of patients in whom a single pathological cause appears to underlie both their epilepsy and features of OCD. There are case reports of patients whose seizures have taken the form of forced thoughts with a quality resembling the obsessions of OCD. Levin B et al, suggested a common lesion in both these states[17].

Aggressive disorder and episodic dyscontrol:

Bach-Y-Rita et al,[1] described 130 patients presenting with violent behaviour in whom the pattern of disturbance was one of episodic dyscontrol. Seven of these had a known history of TLE, and a total of 25/130 subjects reported a seizure at some time.

Overall it appears that temporal lobe EEG abnormality are associated with episodic dyscontrol in those both with and without epilepsy, suggesting that feelings of dyscontrol and rage are primarily associated with discharges in the amygdala and hippocampus[13].

SOCIAL ISSUES

Perception of stigma among people with epilepsy:

Many surveys show that significant numbers of people with epilepsy feel stigmatized. Scambler and Hopkins[19] found that people with epilepsy had important levels of fear and shame. About one third of patients who married after their seizures began did not tell their prospective spouses about the condition, and another third mentioned it only using the terms like, "attacks", "disease spells" and the like. A research group in Australia found that 24% of diagnosed cases denied they had epilepsy even when they were assured of confidentiality. There is some evidence that concealment itself causes additional problems, ranging from avoidance of social interaction to emotional damage.

Disruption in social functioning:

Persons with epilepsy have a higher prevalence of social problems than those from the general population; problems most commonly found include anxiety, poor self-concept, social isolation, social adaptation and depression.

Problems in living with epilepsy related to social adjustment (e.g. Driving and lack of employment opportunities) are also frequently reported in adults with epilepsy. Social problems are important because they have been found to be related to mental health problems such as depression, anxiety and psychopathology in persons with epilepsy[11].

Factors associated with social problems:

Severe and frequent seizures**D**
Presence of other conditions/deficits
Academic underachievement
Chronic condition
Negative attitudes towards epilepsy
Lack of a supportive family environment

CONCLUSION

Apart from physical damage; the emotional, cognitive and social aspect of an epileptic patient is better taken care of through psychological problem oriented therapy. A comprehensive assessment needs to be carried out on a regular basis to facilitate early identification of psychiatric issues, social problems and referral for the rehabilitation services whenever required. Recent data has shown that epileptic patients have gained confidence in life, good self-esteem, emotional stability and social strength through psychological approach.

Patients and their families who have difficulty in understanding the illness, its consequences and who as a result lose their full potential in terms of occupation, living arrangements and behaviour require effective management. More potential discussions and formal psychotherapy could be tailored singly or in groups. Non-specialists counselling can be provided by resources available in schools, colleges, and community health centers. In case of children with epilepsy, family therapy may be needed to unravel and improve complicated family dynamics in order to optimize the quality of life in both patients and parents along with other siblings.

Counselling needs to be integrated with social work, psychological and psychiatric input to take care of associated problems like impaired language comprehension, depression and aggressive outbursts that threaten the break up of the family unit.

Social skill programs and rehabilitation are also need to be provided, particularly in children and adults who exhibit associated neurological problems including mental retardation. Psychological counseling in children with epilepsy should include all aspects of self and environmental issues. Undue restriction and withdrawal from social life are better managed through psychosocial concern and special educational process.

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Laparoscopic colorectal surgery – Current Perspective

After Philip Mouret did first laparoscopic cholecystectomy in 1987, last decade and a half has seen quantum leap in the field of minimal invasive surgery. Technical explosion has revolutionized the face of surgery. All surgical specialties specially abdominal, pelvic and thoracic have seen application of minimal invasive surgery for almost all diseases. Colorectal malignancies have not been an exception. Jacob did first laparoscopic assisted colectomy in 1991. Soon after promising start laparoscopic colorectal surgery was seen with wide skepticism because of some initial reports of port site metastasis in otherwise potentially curable diseases. Since then laparoscopic assisted colectomy was subjected to intense scrutiny and was restricted to be done under trial in most part of USA and Europe.

Laparoscopic colectomy or proctectomy can be done total laparoscopically, laparoscopic assisted or Hand assisted depending upon expertise, stage of the disease and usage of staplers. If an operation can be completed with ease in reasonable time then total laparoscopy is the most minimal invasive approach. This would require a small incision to deliver the specimen or to exteriorize the bowel end. We can use this incision to devascularize, resect and anastomose the bowel outside after initial mobilization of bowel laparoscopically. We can also utilize this incision if made in the early part of the surgery to put hand inside to aid dissection, retraction and hemostasis. This not only shortens the operating time but bridges the gap between conventional and laparoscopic surgery by shortening the learning curve.

Some of the concerns were port site metastasis, clear margins, adequate number of lymph nodes yield, local and distant spread of disease.

Several initial non randomized trials have shown that laparoscopic assisted colectomy is safe, less painful, decreases hospital stay, early return to work with no oncological concerns. Various randomized trials such as COLOR trial, COST trial, BARCELONA trial and HONG KONG trial have published these results. All these trials confirm the short term advantages of minimal invasive surgery as discussed earlier. Long term oncological results are encouraging. Incidence of port site metastasis is a big myth. Literature suggests that the incidence of port site metastasis is close to 1% similar to wound site metastasis in conventional surgery. Number of lymph nodes harvested is similar to conventional surgery. Disease free status of distal and circumferential margins is again comparable to conventional surgery. BARCELONA trial has shown better results for stage III tumors when done laparoscopically. This can be explained on the basis of less immune suppression by laparoscopy. We now know that minimal invasive surgery causes less surgical stress leading to better preservation of immunological and physiological status. In animal models experimental data suggest that laparotomy is associated with significantly increase rate of tumor growth and increase metastasis. As open procedures suppress cell mediated immunity more than laparoscopic surgeries in animal and human beings. The more immunosuppression after a procedure, higher is the morbidity and mortality and also increase cancer response. Therefore a patient who undergoes a laparoscopic procedure is likely to experience less immunosuppression and lesser cancer response as compare to the same procedure done open.

To summarize, laparoscopic colorectal cancer resections are safe and are associated with atleast similar if not better long term survival rates with unchallenged short term advantages of minimal invasive surgery. However, laparoscopic colorectal surgery has a steep learning curve and requires advanced skill in minimal invasive surgery. These procedures today should be restricted to centers with high volume colorectal and minimal invasive work after proper training.

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Drug Regulations Awaiting Enforcement in J&K State

Drug services to common masses and related issues in the state of Jammu and Kashmir are regulated through Drugs and Cosmetics Act, 1940, Drugs and Cosmetics Rules, 1945, Drug Prices Control Order, 1995 and J&K Pharmacy Act, 2011 (samvat). However there are some other drug legislations that either require promulgation in full or demand enforcement of some of their highly significant provisions in the state of Jammu and Kashmir. A few of such drug regulations are discussed as under.

Drugs and Cosmetics Act

Over the past few years, use of drugs belonging to indigenous systems of medicine like Ayurveda, Unani Siddha and Homeopathy has gained wide popularity among masses and a large chunk of population is resorting to these forms of treatment for curing their ailments. J&K State too has witnessed massive growth of sale outlets dealing with drugs belonging to one or more of these systems of medicine. However surprisingly there are absolutely no legal or statutory provisions and mechanisms in place to control, govern, monitor and regulate the sale, storage or distribution of such drugs or licensing of such drug sale outlets. As a result mushroom growth of unlicensed sale outlets has become a big nuisance along the length and breadth of the state of J&K

Drugs and Cosmetics Act, 1940 and Rules thereunder were promulgated in the state of J&K in early seventies. Though provisions relating to the manufacture, sale, storage and distribution of such drugs do exist under chapter IV-A and chapter VI-A of the Drugs and Cosmetics Act of 1940, same have not been enforced unlike other provisions relating to the drugs belonging to allopathic system of medicine. Therefore it should be a priority of the state govt. to bring drug sale, storage and distribution of alternative systems of medicine also under the ambit of Drug and Food Control Organization and enforce the provisions relating to their sale and usage. Adequate powers should be vested upon the existing staff in this regard until further augmentation is made possible. Further the provisions of Drugs and Cosmetics Act, 1940 dealing with manufacture, sale, storage and distribution of cosmetics also need to be enforced to the possible extent in due course of time.

Pharmacy Act

Just the way central Drugs and Cosmetics Act, 1940 has been enforced in the state, central Pharmacy Act of 1948 too needs to be promulgated in place of J&K Pharmacy Act 2011 (samvat). This will bring all pharmacy academic institutions of the state under the purview of the Pharmacy Council of India, help our pharmacists get registered in the Central Register and practice pharmacy profession anywhere in India. Besides it will also enable our pharmacy institutions seek financial assistance from central councils, organize and participate in their continuing education programmes, seminars etc and achieve national and international level standards in our pharmacy and health education.

The Jammu and Kashmir Pharmacy Council has been constituted a few years ago. So far, Council has prepared the first and subsequent registers of those pharmacists who have been carrying on the business or profession of pharmacy in J&K. As a next step, it has to frame an Executive Committee and regulate pharmacy education in the state by way of enforcement of Education Regulations as provided under section 10 of the J&K Pharmacy Act 2011 (samvat). Thereunder it can prescribe the minimum standards of education required for qualification as a pharmacist and can also prescribe the nature and period of study and of practical training to be undertaken before admission to the qualifying examination for a degree or diploma in pharmacy. Further these regulations shall also lay down the subjects of examination and the standards to be attained therein apart from the equipment and facilities to be provided to students for undergoing such approved courses of study.

Once Education Regulations come into force, no person other than a diploma or a degree holder in pharmacy should be designated or registered as a pharmacist and a target date should be fixed beyond which no person other than a pharmacy degree or diploma holder could apply for a drug sale license. Drug trade should thereafter be strictly restricted to diploma or degree holders in pharmacy only. In order to cater to the requirement of qualified pharmacy personnel for such endeavor, diploma course in pharmacy may be commenced at govt. polytechnics in Jammu and Srinagar after appointing teaching staff and making other necessary facilities available for the purpose.

Wider participation of the pharmacy professionals drawn from various sections like academia, clinical set up, regulatory affairs, industry as well as sales and marketing in the affairs of the J&K Pharmacy Council shall pave way for its better functioning, improved outcome and greater acceptance of its policies. Its working should not be confined to any one department of the state administration. Since its decisions affect the entire profession, it calls for a broader representation to all concerned as is true with state pharmacy councils of all other states.

After constituting its Executive Committee and enforcing Education Regulations in the state, J&K Pharmacy Council may appoint its own inspectors having prescribed qualifications, as provided under section 26 A of the Pharmacy Act, 1948 in order to inspect the premises where drugs are dispensed, to enquire whether a person who is engaged in selling, dispensing or compounding of drugs is a registered pharmacist, to investigate complaints regarding contravention of the Act and to institute prosecutions against the offenders. This initiative shall help our society get rid of drug delivery and distribution at the hands of unqualified, unregistered and unscrupulous people.

Narcotic Drugs and Psychotropic Substances Act

Reports of widespread drug addiction and abuse of prohibited medicines have been pouring in from various parts of the state over the last few years. A tough and stringent piece of legislation namely Narcotic Drugs and Psychotropic Substances Act has been enacted in 1985 to help curb the scourge of drug abuse. Act is a central Act and extends to the state of Jammu and Kashmir too. Most significant feature of the Act is the exemplary punishment provided for most of the offences;in some cases rigorous imprisonment upto 30 years in addition to a fine of more than 3 lacs of rupees. Even mere possession of a small quantity of any narcotic drug or psychotropic substance as listed in the Act for an unauthorized personal use or consumption of such drug are cognizable offences under this Act.

The Act is however chiefly enforced by the Narcotics Control Bureau whose workforce is very meager and needs expansion. Though this Bureau has a nodal centre at Jammu, there is none in the valley making its activities imperceptible. More people possessing degrees in Pharmaceutical Sciences need to be appointed as enforcement officers under the Act for an efficient and foolproof administration of its provisions. Sale, storage and use of drugs specified under Schedule X of the Drugs and Cosmetics Act, 1940 has to be regulated with a greater vigil by the inspectorate working under Drug Control Organization. Record-keeping of such drugs should be

made indispensable and the same should be checked regularly by the inspectorate. License to sell, stock and distribute drugs pertaining to Schedule X should be restricted to dealers with absolutely spotless track record and those indulging in unlawful trade of such drugs should be severely punished as per law.

Drugs and Magic Remedies Act

With a view to curb the menace of false and misleading advertisements and to prohibit advertisements of certain remedies alleged to possess magical curative properties that are likely to make the ignorant ones resort to self-medication or quackery, the Drugs and Magic Remedies Act was passed in 1954. However the Act extends to the state of J&K only to a limited extent. It needs to be enforced in toto and necessary powers towards its enforcement should be delegated fully to the available manpower that is competent for the same. Ethical criteria for drug promotion and advertising should be established for the state of Jammu & Kashmir along the lines of such ethical criteria developed by the World Health Organization. Drug promotional activities not in accordance with the law may not be permitted in the state. This will help to protect the public from being exploited.

MCI Guidelines

Guidelines put forth by the Medical Council of India with regards requirement of qualified pharmacists in hospitals need to be implemented. They have prescribed a minimum of three qualified pharmacists for every 50 bed-hospital or less, 5 for 51-100 bed hospital, 8 for 100-200, 10 for 200-300 and a minimum of 15 qualified pharmacists for 300-500 bed hospitals. National Human Rights Commission in its report on hospital pharmacy services submitted in January, 1999 has also recommended that, "every hospital should organize the pharmaceutical activities in regard to purchase, storage, testing, compounding, dispensing and distribution of drugs under the charge of a competent and experienced persons possessing at least degree in pharmacy". In accordance with these guidelines and the recommendations made vide Hathi Committee Report (1975), it is necessary that the requirements as per MCI guidelines be fulfilled and necessary mechanism devised.

Further such positions should be exclusively reserved for trained pharmacy graduates and the services of at least one pharmacy graduate should be made available at every primary health centre, sub-district and district hospital of the state. It is only professionally trained and legally qualified pharmacy personnel who could counsel and disseminate information to patients on matters like indications of the drug, its contra-indications, adverse effects, precautions, dosage etc and could also play their legitimate and pivotal role in procurement, testing, storage and dispensing of standard quality drugs in every hospital and primary health centre.

State Drug Policy

As a result of increasing complexity of pharmaceutical and healthcare services in the state in the wake of an overwhelming increase in the number of drug sale outlets, an unexpected surge in the morbidity rate, greater number of people resorting to alternative systems of medicine, need for promulgation of a comprehensive drug policy in the state has become inevitable.

Formulation of a new drug policy in the state also assumes immense importance in order to invoke an effective quality control system for drugs, ensure rational prescribing and use of medicines, make safe and effective drugs available in adequate quantities particularly at govt. centers, improve procurement, storage and distribution practices for drugs and other medical supplies, provide quality pharmaceutical and healthcare services at hospitals, stringently enforce all drug-related laws, extend adequate research and training facilities at all academic and healthcare institutions and to initiate indigenous manufacture of life saving drugs within the state. All these vital components of our basic healthcare need to be guided by a strong framework of guidelines envisaged under a proper policy statement.

Given the kind of training and technical know-how of pharmacy graduates, they provide a better choice than simple science graduates in dealing with health related issues concerning the community at large. With their knowledge base on community health education, they are more suited for the posts of community health officers. Hence the minimum qualification for the post of community health officers may be proposed as a bachelor's degree in pharmacy rather than simple graduation in science as is currently in vogue.

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